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2025 ESC Clinical Consensus Statement on mental health and cardiovascular disease: developed under the auspices of the ESC Clinical Practice Guidelines Committee

Developed by the task force on mental health and cardiovascular disease of the European Society of Cardiology (ESC)

Endorsed by the European Federation of Psychologists' Associations AISBL (EFPA), the European Psychiatric Association (EPA), and the International Society of Behavioral Medicine (ISBM)

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Patient Forum

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Abbreviations and acronyms

ACE	Adverse childhood experience
ACHD	Adult congenital heart disease
ACS	Acute coronary syndrome
ACTIVE	Acknowledge, Check, Tools, Implement, Venture, Evaluate
AF	Atrial fibrillation
AMI	Acute myocardial infarction
CABG	Coronary artery bypass graft
CAD	Coronary artery disease
CBT	Cognitive-behavioural therapy
CDI-PTSD	Cardiac disease-induced post-traumatic stress disorder
CDI-SF	Cardiac Distress Inventory-Short Form
CHD	Coronary heart disease
CI	Confidence interval
CODIACS-QoL	Comparison of Depression Interventions After Acute Coronary Syndrome: Quality of Life
CV	Cardiovascular
CVD	Cardiovascular disease
EAPC	European Association of Preventive Cardiology
EASD	European Association for the Study of Diabetes
ECG	Electrocardiogram
ECR	Exercise-based cardiac rehabilitation
eHealth	Information and communication technologies for health
EMDR	Eye movement desensitization and reprocessing
ESC	European Society of Cardiology
GAD	Generalized Anxiety Disorder
HADS	Hospital Anxiety and Depression Scale
HDL	High-density lipoprotein
HF	Heart failure
HF-ACTION	Heart Failure-A Controlled Trial Investigating Outcomes of Exercise Training
HR	Hazard ratio
HRQoL	Health-related quality of life
HTx	Heart transplantation
ICD	Implantable cardioverter-defibrillator
IES	Impact of Event Scale
IHD	Ischaemic heart disease
INOCA	Ischaemia with non-obstructive coronary arteries
LDL	Low-density lipoprotein
MACE	Major adverse cardiac events
MAOI	Monoamine oxidase inhibitor
mHealth	Mobile health
MI	Myocardial infarction
MINOCA	Myocardial infarction with non-obstructive coronary arteries
MotInt	Motivational interviewing
NYHA	New York Heart Association
OCEAN	Omega-3 Supplementation for Co-Morbid Depression and Heart Failure Treatment
OHCA	Out-of-hospital cardiac arrest
OR	Odds ratio
PAH	Pulmonary arterial hypertension
PCI	Percutaneous coronary intervention
PH	Pulmonary hypertension
PHQ	Patient Health Questionnaire
PTSD	Post-traumatic stress disorder
PTSS	Post-traumatic stress symptom
QoL	Quality of life
RCT	Randomized controlled trial
RR	Risk ratio
SCAD	Spontaneous coronary artery dissection
SCD	Sudden cardiac death
SDM	Shared decision-making
SES	Socioeconomic status
SMI	Severe mental illness
SNRI	Serotonin and norepinephrine reuptake inhibitor
SSRI	Selective serotonin reuptake inhibitor
SSS	Subjective social status
SWB	Subjective well-being
TCA	Tricyclic antidepressant
TTS	Takotsubo syndrome
VAD	Ventricular assist device
WHO	World Health Organization

1. Preamble

ESC Clinical Consensus Statements, developed under the auspices of the ESC Clinical Practice Guidelines Committee, evaluate and summarize available evidence with the aim of assisting health professionals in proposing the best diagnostic or therapeutic approach for an individual patient with a given condition. ESC Clinical Consensus Statements are intended for use by health professionals but do not override their individual responsibility to make appropriate and accurate decisions in consideration of each patient's health condition and in consultation with the patient or the patient's caregiver where appropriate and/or necessary. It is also the health professional's responsibility to verify the rules and regulations applicable in each country to drugs and devices at the time of prescription and to respect the ethical rules of their profession.

ESC Clinical Consensus Statements represent the official position of the ESC on a given topic. ESC Policies and Procedures for formulating and issuing ESC Guidelines and documents developed under the

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auspices of the ESC Clinical Practice Guidelines Committee can be found on the ESC website (https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Guidelines-development/Writing-ESC-Guidelines).

This Task Force was selected by the ESC to include professionals involved with the medical care of patients with this pathology and to include patient representatives and methodologists. The selection procedure included an open call for authors and aimed to include members from across the whole of the ESC region and from relevant ESC Subspecialty Communities. Consideration was given to diversity and inclusion.

Clinical consensus statement Task Forces perform a critical review and evaluation of the published literature on diagnostic and therapeutic approaches including assessment of the risk–benefit ratio. Evidence tables summarizing key information from relevant studies are generated to facilitate the formulation of management consensus statements, to enhance their comprehension after publication, and to reinforce transparency in the clinical consensus statement development process. The tables are published in their own section of the ESC Clinical Consensus Statement and reference specific recommendation tables.

After an iterative process of deliberations, a modified Delphi process on all management consensus statements was conducted. The Task Force members ranked their level of agreement or disagreement with each management consensus statement using the Likert ordinal scale: strongly agree, agree, neither agree nor disagree, disagree, strongly disagree, recuse. Consensus of agreement was inferred if >75% of the respondents selected the options 'strongly agree' or 'agree'.

The writing and reviewing panels provided declaration of interest forms for all relationships that might be perceived as real or potential sources of conflicts of interest. Their declarations of interest were reviewed according to the ESC declaration of interest rules which can be found on the ESC website (http://www.escardio.org/doi) and were compiled in a report published in a supplementary document with the Clinical Consensus Statement. Funding for the development of ESC Clinical Consensus Statements is derived entirely from the ESC with no involvement of the healthcare industry.

The CPG Committee supervises and co-ordinates the preparation of new clinical consensus statements and approves their publication. In addition to review by the CPG Committee, ESC Clinical Consensus Statements undergo multiple rounds of double-blind peer review on a dedicated online review platform. The review is conducted by topic experts, including members from ESC National Cardiac Societies and from relevant ESC Subspecialty Communities. Guideline Task Forces consider all review comments and are required to respond to all those classified as major. After appropriate revisions, Task Force and the CPG Committee members approve the final document for publication in the *European Heart Journal*.

Unless otherwise stated, ESC Clinical Consensus Statement content refers to sex, understood as the biological condition of being male or female, defined by genes, hormones, and sexual organs. Off-label use of medication may be presented in this Guideline if a sufficient level of evidence shows that it can be considered medically appropriate for a given condition. However, decisions on off-label use must be made by the responsible health professional giving special consideration to ethical rules concerning healthcare, the specific situation of the patient, patient consent, and country-specific health regulations.

2. The scope of this consensus statement

This consensus statement provides readers with insights into the extent and magnitude of the impact of mental health on cardiovascular disease (CVD) and vice versa. It also outlines how the negative impacts of this reciprocal relationship can be prevented or minimized. Clinical cardiovascular (CV) practice often overlooks the impact of mental health and the importance of its inclusion in CV care; this needs to change. Therefore, this consensus statement sets out to be broad and ambitious. The high burden of concomitant CVD and mental health conditions requires a new integrated approach to caring for people with CVD. Cardiovascular health professionals need to develop collaborations with mental health professionals to provide guidance for practice and appropriate support for people with CVD and their caregivers. Whilst challenging, healthcare professionals are encouraged to pursue the implementation of the suggestions in this statement, regardless of their profession, clinical setting, or resources. Changes in the current models of care, with structure and resource adjustments, may require both centre-specific and country-specific measures. Consequently, the document adopts a global perspective and reviews the evidence on the association between mental and CV health, as well as tackling key aspects such as awareness, communication, screening, optimal management, stigma, gaps in evidence, and needs for research. A comprehensive and inclusive perspective has also prompted the use of respectful language in healthcare.[1] People with lived experience of CVD and mental health conditions have been central in the creation of this document, and their perspectives underpin the importance of changing practice, and emphasize the need for implementation of the steps suggested in this statement.

2.1. Methods employed in the consensus statement

This consensus document involved a multidisciplinary team of cardiologists, nurses, general professionals, psychologists, psychiatrists, geriatricians, and people with experience of mental health and CV conditions. It was developed under the auspices of the ESC Clinical Practice Guidelines Committee. The Task Force Chairs proposed the document structure; this was subsequently refined through group input, with section leaders ensuring consistency, coherence, and clinical relevance. Literature reviews are comprehensively presented within evidence tables. Relevant, clinically tangible information is summarized within the text for the benefit of the clinical professional. Multiple meetings were held to discuss the available evidence and the relative strength of that evidence.

On the basis of the evidence reviews and discussion, the Task Force identified that there is limited evidence to guide practice, despite the clear and important multidirectional interaction between mental health and CVD. As a result of the dearth of research, the Task Force adopted a modified Delphi process to generate main recommendations. The modified Delphi process is a structured communication technique that allows a group of experts to gather opinions on a given complex or controversial topic, for which there is insufficient evidence or incomplete knowledge.[2] The modified Delphi questionnaire included management consensus statements. These statements summarize factors from each section and typically consist of actions or practical suggestions that healthcare professionals should endeavor to implement in their practice. As these are based on limited evidence, the Task Force members ranked their level of agreement or disagreement with each management consensus statement using the Likert ordinal scale: strongly agree, agree, neither agree nor disagree, disagree, strongly disagree, recuse. Consensus of agreement was inferred if >75% of the respondents selected the options 'strongly agree' or 'agree'. Consensus was reached for all the proposed management consensus statements following the

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first round of voting. A total of 34 management consensus statements are presented in this document. Section summary points represent important components of the section that a healthcare professional should be aware of. They were also reviewed and revised by the Task Force, to ensure that they reflected the key elements of each section. Section summary points and management consensus statements are presented at the end of each section.

3. Introduction

3.1. The relationship between mental and cardiovascular health and disease

Mental health is an integral component of a person's health. According to the World Health Organization (WHO), mental health is a state of mental well-being that enables people to cope with the stresses of life, realize their abilities, learn well and work well, and contribute to their community.[3] Despite its importance, there is not a single agreed definition for mental health.[4]

Although mental health and mental illness are sometimes considered as dual continua, for the purpose of this document, mental health is an overarching concept of a complex continuum spanning from optimal mental health with dominant features such as optimism, resilience, and well-being, to negative mental health states including severe mental illness (*Figure 1*).[5] The nomenclature surrounding negative aspects and mental health disturbances also lacks consistent definitions. Mental health condition is a wide term that will be used in this document to refer to psychosocial difficulties and other mental states associated with distress, impairment in cognitive functioning, altered emotional responses, altered behaviour, and risk of self-harm. Within mental health conditions, mental health disorders refer to mental health states characterized by a clinically significant disturbance in an individual's cognition, emotional regulation, or behaviour, usually associated with distress or impairment in important areas of functioning.[3] Mental health disorders include severe mental illnesses (SMI) defined by a significantly impaired level of psychosocial functioning (*Figure 1*).[6] In relation to the latter, we have drawn upon definitions and diagnostic criteria for mental health conditions that are specified in the International Classification of Diseases for Mortality and Morbidity Statistics, Eleventh Revision.[7] Organic mental health disorders, such as cognitive impairment and dementia, are outside the scope of this document.

This consensus statement will address mental health conditions across the spectrum of severity and type, as both people with symptoms of suboptimal mental health identified through screening, and people with manifest mental health disorders, are at high CVD risk. Core principles, across the spectrum of disease, are outlined. To illustrate the impact and implementation of some of the key aspects of the document, the narratives of people living with CVD and clinical cases have been incorporated into the online document 'Clinical cases and patient perspectives'.

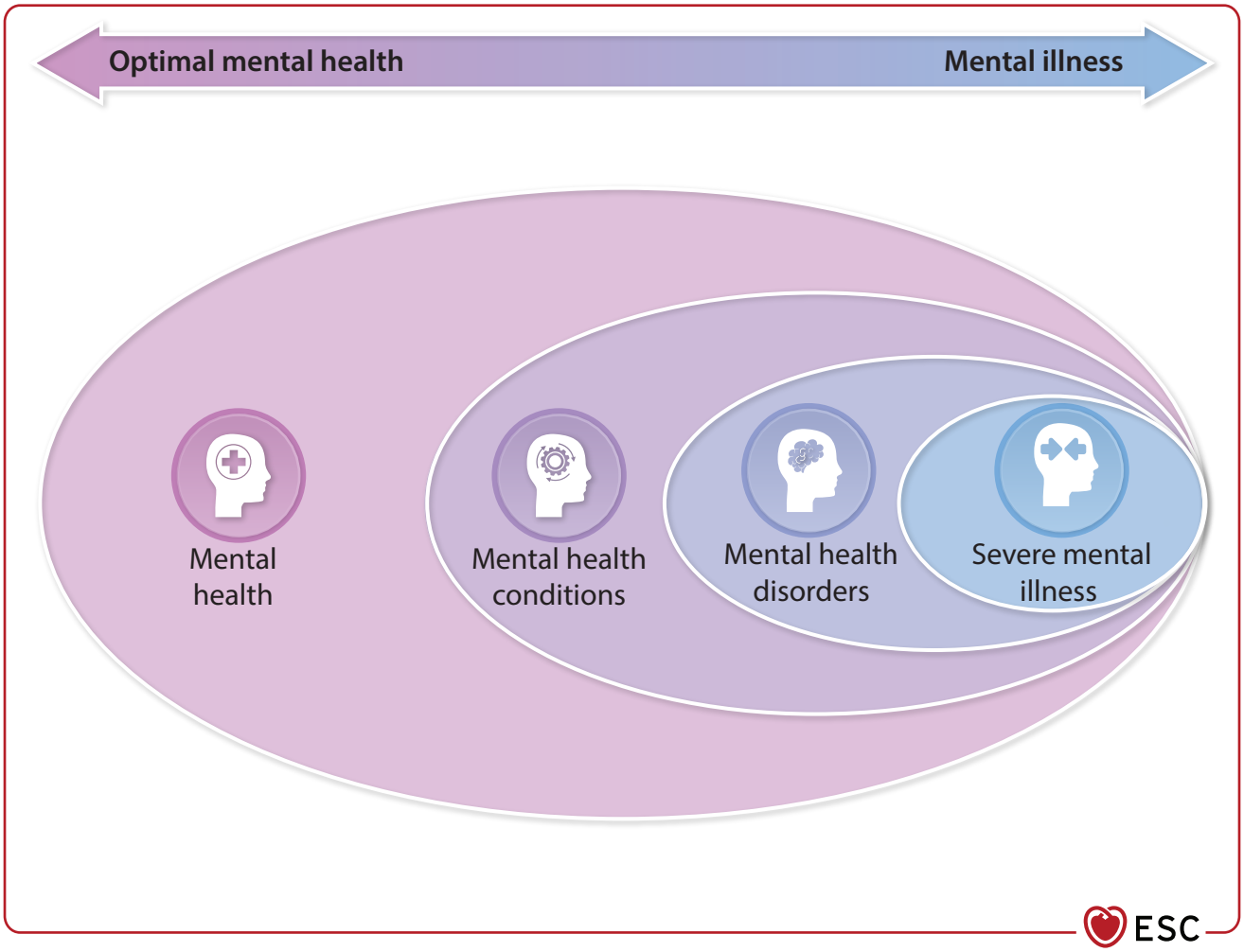

Figure 1 Concept of mental health within this consensus statement.

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Mental health and mental health conditions interact with CV health (defined as the health of the heart and blood vessels)[8] and CVD in a multidirectional way (*Figure 2*). For example:

- Positive features of mental health at an individual and societal level are associated with better CV health,[9–11] while people with mental health conditions are more likely to be at greater risk of CVD.[12]
- Acute CV events or chronic CVD impact on mental health, worsening pre-existing mental conditions or triggering new conditions.[13–16]
- The concurrence of CVD and mental health conditions may interact, worsening both mental health and CV prognosis.[17–19]
- People with mental health conditions are often the most disadvantaged, experiencing social and economic hardship as well as dealing with stigma, stereotypes, and prejudice.[20]
- People with mental health disorders, particularly SMI, are more vulnerable, and are less likely to receive the same diagnostic and treatment efforts as persons without mental health conditions.[21–26]

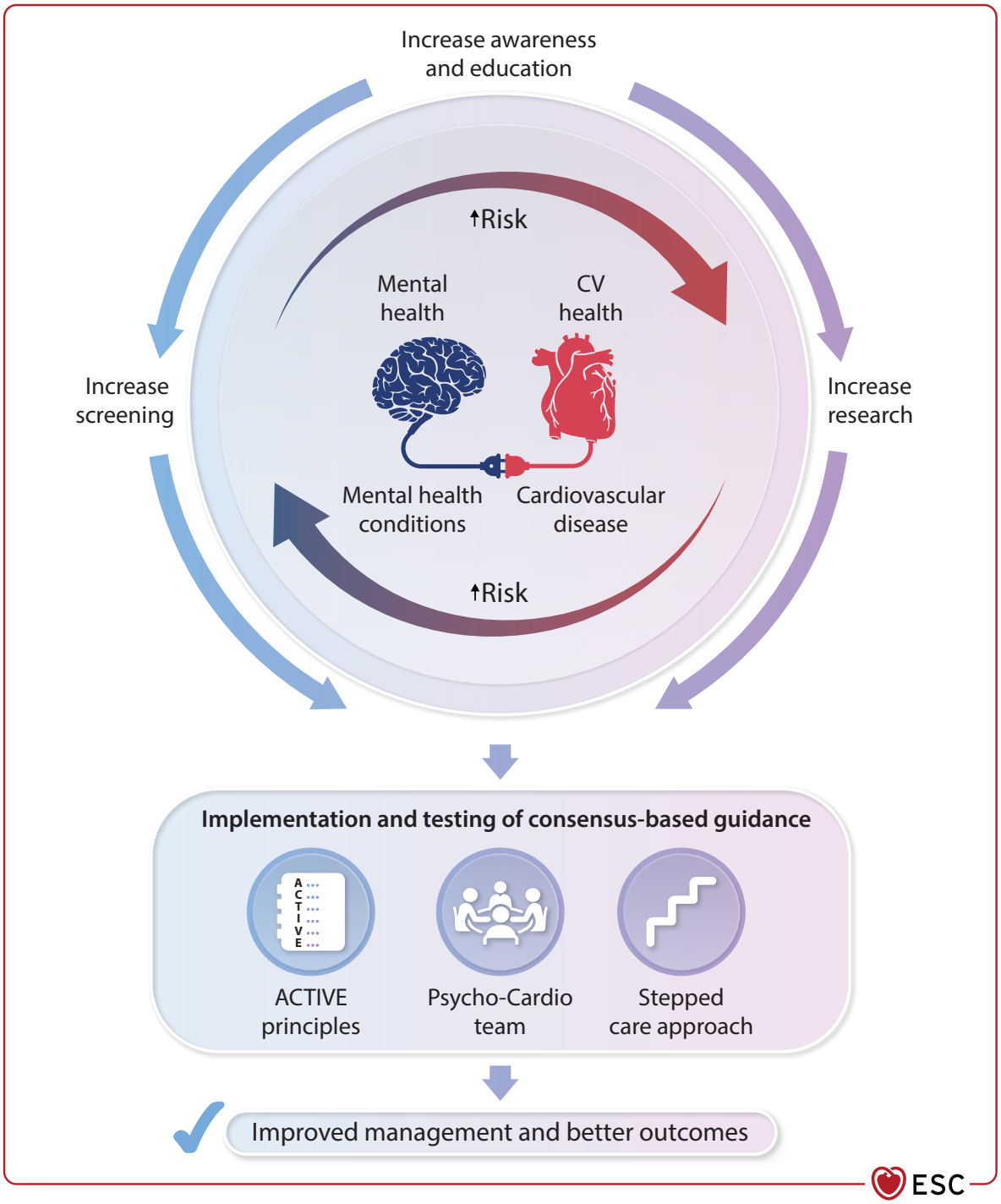

Figure 2 Mental/cardiovascular health, disease interaction, and future directions. CV, cardiovascular. ACTIVE, **A**cknowledge, **C**heck, (use validated) **T**ools, **I**mplement, **V**enture, **E**valuate (see *Figure 4*).

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3.2. Enduring problems

Despite the strong association between mental health, CV health, and CVD, and its clinical relevance, there are multiple problems (*Figure 2*) including:

- Insufficient awareness among healthcare professionals of the prevalence of mental health conditions in the population and their impact on increasing risk of developing CVD.[27]
- Limited appreciation among healthcare professionals of the incidence and prevalence of mental health conditions and mental disorders among people with CVD and their impact on quality of life (QoL), therapeutic adherence, and CVD prognosis.[27]
- Inadequate recognition of the stigma of SMI in society and in healthcare, and its consequences for people coping with SMI, their family, and caregivers.[28]
- Lack of systematic and appropriate screening, evaluation, communication, and management of mental health, which are not integrated in routine clinical CV practice.[29]
- Little knowledge and ongoing research about how to improve CV health and prevent CVD in people with mental health conditions and mental disorders.[21–23,27]
- Limited evidence and ongoing research on the best ways to communicate, promote, maintain, and improve mental health and resilience in people with CVD and their family members.[30]
- Little guidance about how to improve the care of people with SMI, despite strong evidence that people with SMI and CVD have worse CV prevention, acute and chronic care, and prognosis.[21,24–26]
- Limited awareness of the importance of family and caregivers and their needs, as both CVD and mental health conditions affect a person's wider social network.[31–34]

Cardiovascular care is optimal when it is person-centred and seeks to improve overall health, not only CV but also mental health, as an integral component. This approach needs to be integrated into routine practice as most current models of CV care do not consider mental health as a primary goal. To achieve this, healthcare professionals need more comprehensive information about mental health and how to deliver mental health sensitive, person-centred care. Furthermore, the mental health challenges experienced by family members and caregivers are often not recognized nor addressed.[35] Central to this statement is the recognition that CV care professionals need to develop collaboration with mental health professionals in order to ensure optimal care and outcomes. Access to mental health services may vary, but the multidisciplinary CV team needs to include a collaborating mental health professional, psychologist, or psychiatrist to provide guidance for practice and appropriate support for people with CVD and their caregivers. In this consensus statement, we have called this the Psycho-Cardio team (*Figure 3*).

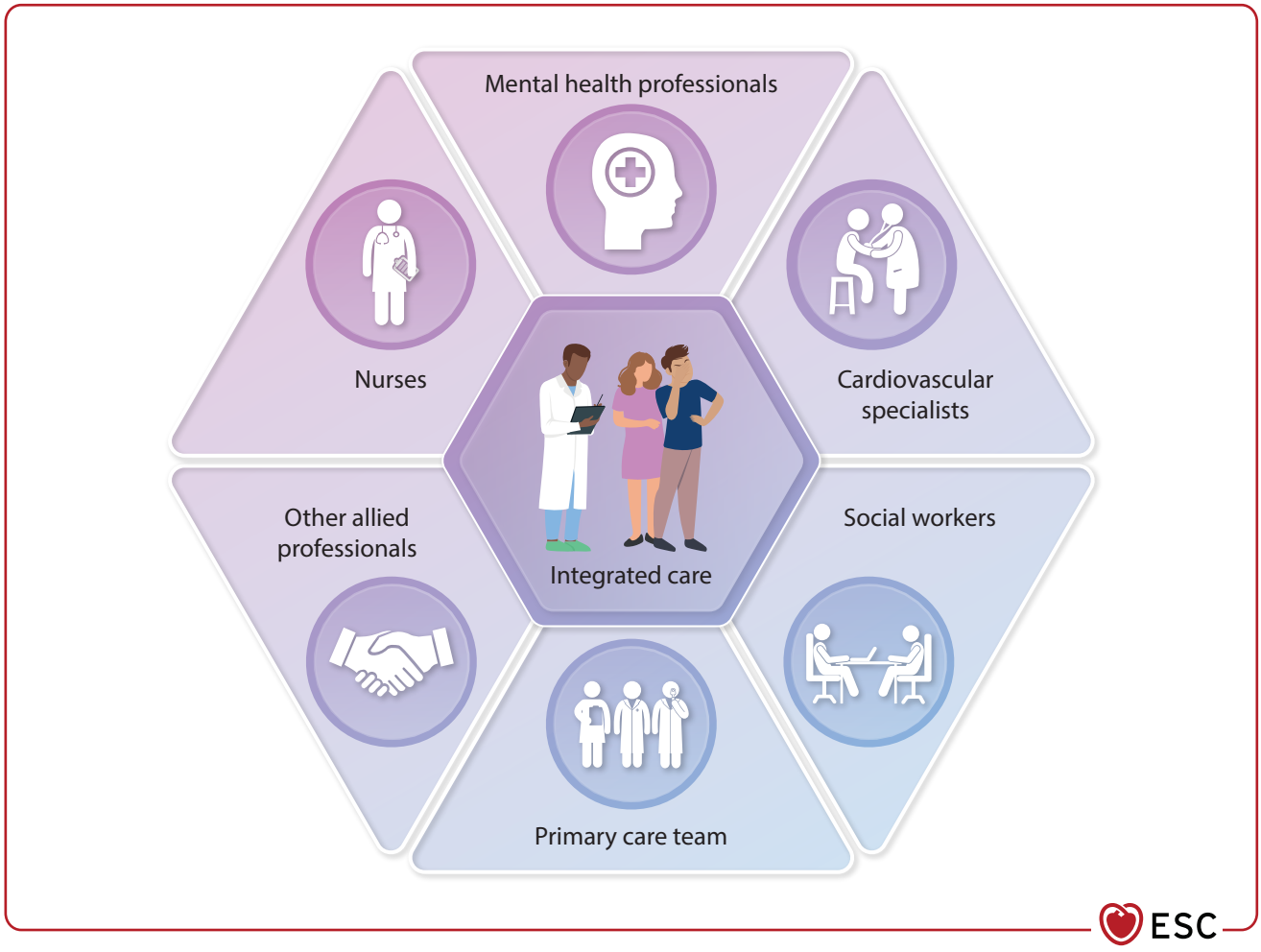

Figure 3 The Psycho-Cardio team.

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3.3. Aims of the document

This document adopts a broad, summarizing approach, and provides key and consensus statements which collectively:

- Critically review the evidence on the association between mental and CV health.
- Increase awareness of the clinical importance of the association between mental and CV health.
- Increase awareness and combat the stigma of mental health conditions and mental health disorders.
- Promote increased mental health screening and better management for people with CVD and mental health conditions and support for caregivers.
- Provide guidance on initial clinical, systemic, and organizational changes needed, as well as signposting future directions.
- Identify gaps in evidence and research needed to improve the care for people with mental health conditions and CVD.

3.4. The Psycho-Cardio team

Multidisciplinary teams are needed to offer a holistic approach to health promotion and management in people with CVD and mental health conditions. In addition to CV and mental health professionals, the Psycho-Cardio team should be augmented by allied professionals, as appropriate.[36] Care continuity should be ensured via co-ordination with the multidisciplinary primary care team, and psychosocial determinants and potential social interventions discussed with social workers and relevant professionals. All professionals should advocate for improved mental health and CV care; those with advocacy responsibilities within the public health and policy domain should ensure changes recommended here are priorities. A practical approach to change routine clinical CV care towards being more person-centred is to focus on awareness toward the person with CVD and caregivers' mental health, CV prevention, and care of people with mental health conditions following the ***ACTIVE principles*** (*Figure 4*).

- First, *acknowledge* (**A**) the intricate relationship between mental health, CV health, and CVD, their common and specific determinants, and the influence that mental health conditions may have on prognosis and care equity. Particular attention is required to identify and eliminate potential bias, disparities and stigma associated with mental health conditions and disorders, particularly in those with SMI.
- Second, *check* (**C**) systematically for the presence of symptoms of mental health conditions or mental health disorders at CV visits, and check CV risk factors during mental health visits.
- Third, use validated *tools* (**T**) to assess mental and CV health status among people with CVD, and use tools to inform and educate about the importance of mental and CV health, and their relationships.

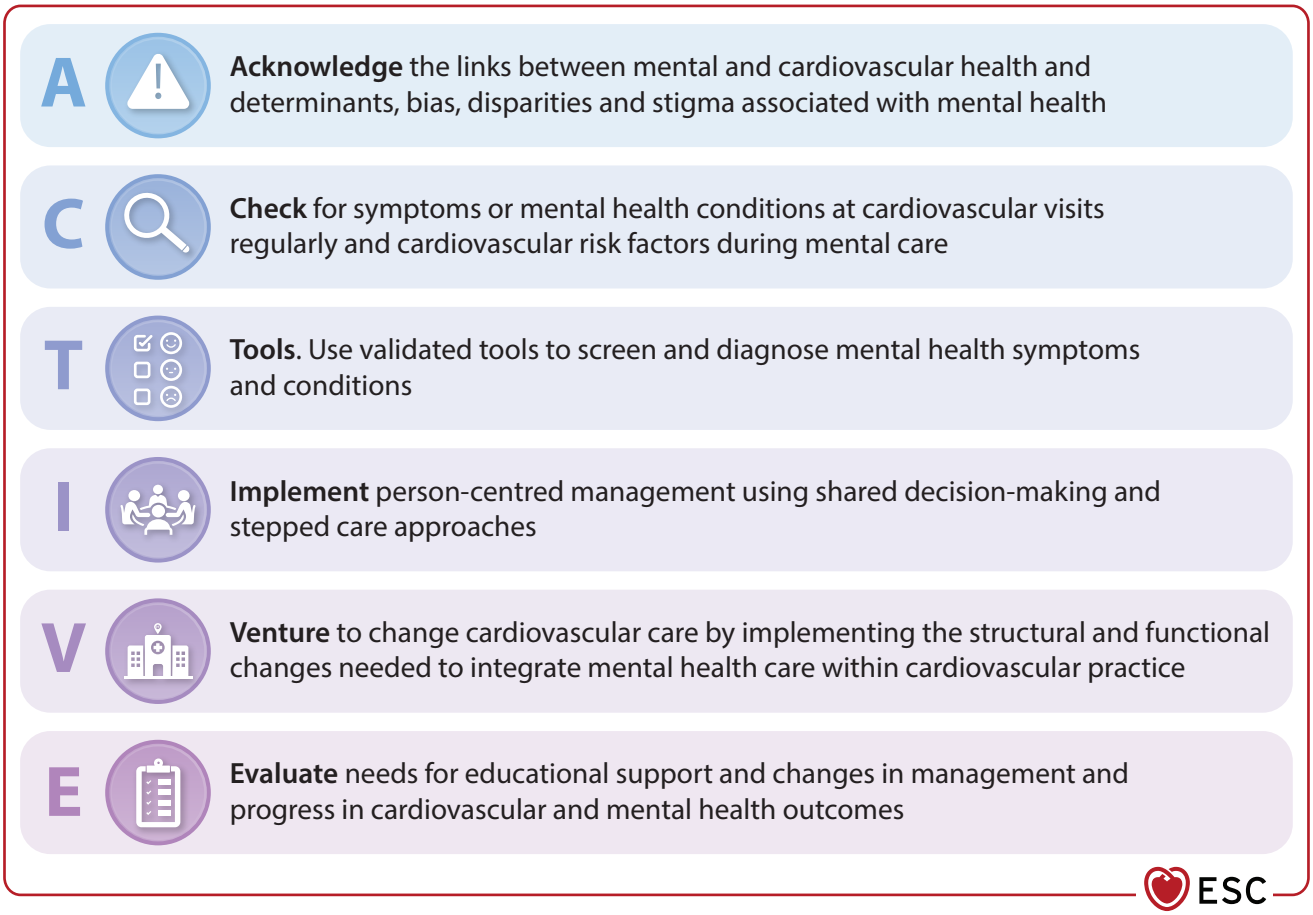
A
Acknowledge the links between mental and cardiovascular health and determinants, bias, disparities and stigma associated with mental health
C
Check for symptoms or mental health conditions at cardiovascular visits regularly and cardiovascular risk factors during mental care
T
Tools. Use validated tools to screen and diagnose mental health symptoms and conditions
I
Implement person-centred management using shared decision-making and stepped care approaches
V
Venture to change cardiovascular care by implementing the structural and functional changes needed to integrate mental health care within cardiovascular practice
E
Evaluate needs for educational support and changes in management and progress in cardiovascular and mental health outcomes
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Figure 4 The ACTIVE principles to improve mental health in cardiovascular care.

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- Fourth, *implement* (**I**) person-centred practices in CV care using evidence-based, stepped care approaches. These should be individualized to the person and their circumstances and recognize the importance of caregivers and caregivers' health status.
- Fifth, *venture* (**V**) to convince professionals, managers, and people living with CVD, to obtain their collaboration, support, and resources to make the needed structural and functional changes to face this challenge. These will not occur spontaneously. Professionals and institutions willing to improve CV and mental healthcare through collaborative, person-centred models, with compassionate support for families and caregivers will undoubtedly face several barriers when implementing change.
- Sixth, *evaluate* (**E**) the current status of routine CV care in each setting and estimate the needs for organizational, educational, and clinical support to implement the required changes. Progress in management and mental health outcomes will also have to be evaluated for quality assurance and improvement purposes.

3.5. Section summary points and management consensus statements from *Section 3*

SECTION SUMMARY POINTS	
(i)	Mental health and mental health conditions interact with CV health and CVD in a multidirectional way.
(ii)	The coexistence of CVD and mental health conditions can create a mutual interaction that worsens both mental and CV health, leading to poorer outcomes.
(iii)	Routine CV clinical practice lacks integrated, systematic and appropriate screening, evaluation, communication, and management of mental health.
(iv)	There is limited evidence on the best ways to communicate, promote, maintain, and improve mental health and resilience in people with CVD and their family members.
(v)	The evidence base to guide practice in relation to the screening and management of mental health conditions in people with CVD is limited.
MANAGEMENT CONSENSUS STATEMENTS	
(i)	Cardiovascular care is optimal if it is person-centred and seeks to improve overall health, not only CV but also mental health, as an integral component.
(ii)	A multidisciplinary team including mental health professionals, psychologists, and/or psychiatrists (Psycho-Cardio team) is needed in CV care to provide guidance for practice and appropriate mental health assessment, support, and management to people with CVD and their caregivers.
(iii)	Cardiovascular services should aspire to implement a Psycho-Cardio team approach, tailored to the local population, context, and resources.
(iv)	Implementing the ACTIVE principles is a practical approach to transform routine clinical CV care towards being more person-centred, integrating mental healthcare into routine CV practice to improve care.

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4. Impact of mental health on the risk of developing cardiovascular disease

This section focuses on the relationship between mental health and CV risk in individuals without known CVD. The aim is to elucidate for the healthcare professional the aetiological impact of psychosocial stress factors on the onset of CVD. The evidence, which includes large population-based studies and meta-analyses that adjust or control for concurrent somatic risk factors, is robust. Such evidence underscores the independent impact of psychosocial risk factors on the prediction of hard endpoints including all-cause mortality, and major adverse cardiac events (MACE).

4.1. Positive mental health states as predictors of better cardiovascular health

Subjective well-being (SWB) is an overarching term that covers different aspects of positive mental affect states.[3] An individual with SWB is satisfied with life, has a sense of purpose, and possesses meaning in life.[37] Related features to positive affectivity encompass psychological well-being, high life satisfaction, joy, optimism, and happiness.[38] Sexual health is also an important component of mental well-being and can be impaired both as a cause or as a consequence of mental and CV issues.[39] Positive trait-like dispositions like sense of coherence, a person's view of life, and capacity to respond to stressful situations,[40] and other more psychobiological-driven personality factors (i.e. emotional vitality, vigour, positive energy, and resilience) are further linked concepts employed in population-based studies.

Subjective well-being and related features have been advocated as protective states against premature mortality and morbidity, mainly focusing on CVD conditions. Systematic review and meta-analytic evidence have shown favourable effects on mortality.[41,42] In the largest meta-analysis, the survival impact of SWB was significant in both men and women, however, more protective in men.[42] Positive affect was associated with a lower risk of coronary heart disease (CHD),[43] and optimism with a lower incidence of heart failure (HF).[44] Consecutive studies have demonstrated the importance of sexual well-being in overall well-being in CVD.[39] Lastly, negative affect, a component of SWB, has also been shown to increase incident CVD events, even after controlling for known confounders.[45]

Mechanistically, SWB may have stress-buffering properties that diminish physiological hyper-responsiveness[46] or exert protective CV effects via a more balanced physiology (i.e. autonomic regulation, enhanced neuroendocrine functioning, reduced inflammation).[47] Alternatively, SWB may result in greater engagement in healthy behaviours,[48] that in turn drive better social functioning, personal relationships, and QoL.[49]

4.2. Psychosocial stress

Psychosocial stress arises when an individual perceives and responds to a social demand (family issues, social isolation, financial pressures, and work) that exceeds an individual's adaptive capacity or regulatory homeostatic range to cope.[50,51] The same situation can be stressful for one person but not for another, due to psychological appraisal processes that typically operate outside of conscious awareness.[52] In most cases, psychosocial stress results in an appropriate state of arousal

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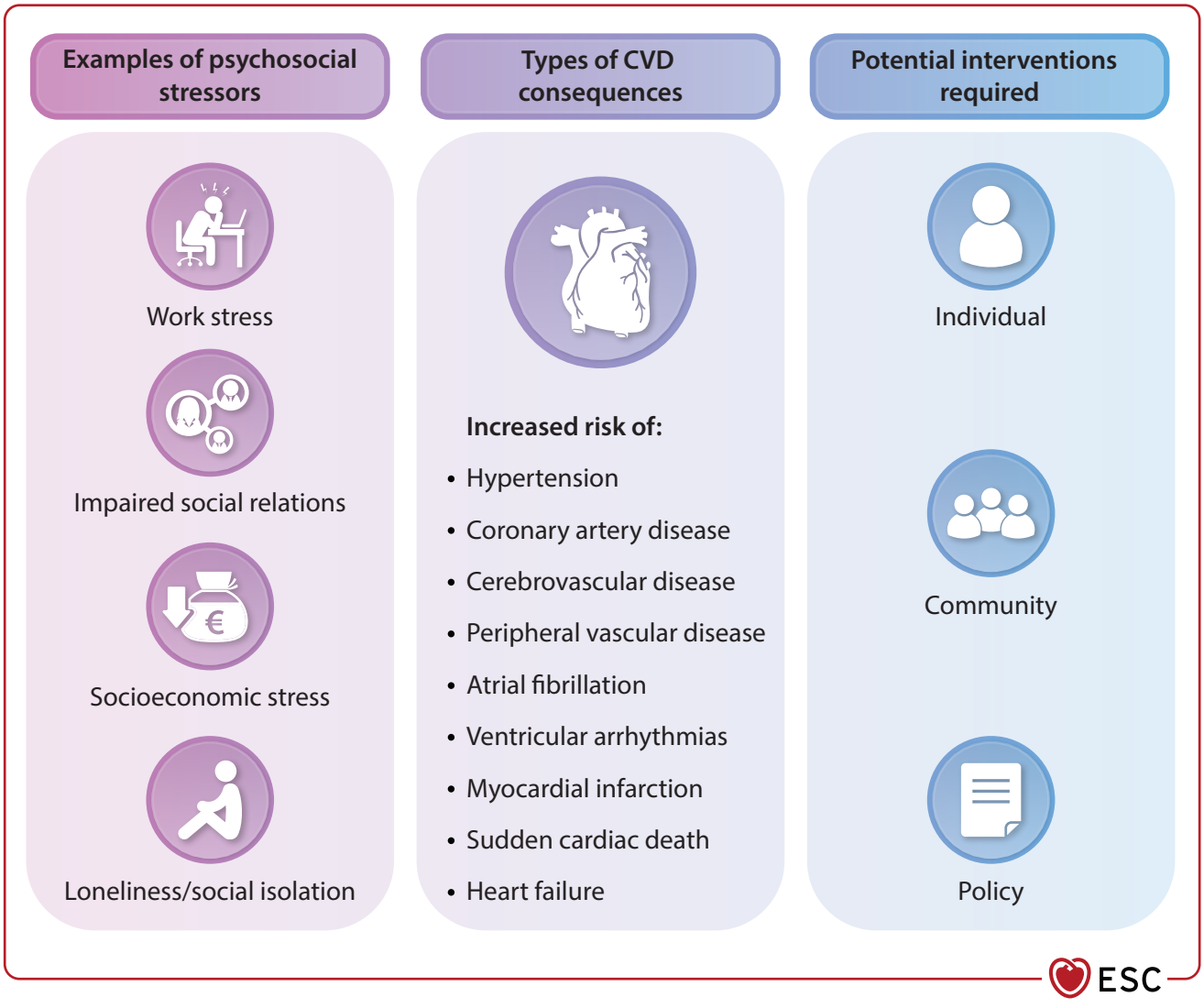

Figure 5 Sources of psychosocial stress as risk factors for cardiovascular disease. CVD, cardiovascular disease.

and hyper-mobilization[53] that is contextually applicable.[52] However, clinically more important are long-term sustained stress conditions (chronic stress) which cause exacerbated pathophysiological changes in the heart and vasculature. Various psychosocial risk factors are described below and illustrated in *Figure 5*.

Psychosocial factors as a whole are as potent risk factors as conventional risk factors, with an adjusted odds ratio (OR) of 2.51 [95% confidence interval (CI) 2.15–2.93].[54] Chronic psychological stress is associated with an increased risk of CVD.[55] People experiencing their first myocardial infarction (MI) reported higher prevalence of stress (work home, financial, major life events) in the 12 months prior to admission; the highest risk was for permanent stress at work (OR 2.14; 99% CI 1.73–2.64). The increased risk is consistent across regions, ethnic groups, men, and women.[56] Stress can trigger CVD events through: (i) changes in autonomic balance, (ii) alteration of neuroendocrine axes, (iii) activation of inflammatory systems, and (iv) engagement in health-damaging behaviours like smoking and alcohol consumption.[57] The latter typically cluster significantly with stress exposure.[57] Management of psychosocial stress and promotion of mental well-being should therefore be integral parts of comprehensive CV healthcare and prevention.

4.3. Work stress and unemployment

Most individuals spend a major portion of their active lives in work environments, which can be a source of psychosocial stress. A large-scale meta-analysis demonstrated that work stress/job strain was significantly associated with a higher risk for CHD.[58] In equally large prospective cohort studies, job strain was associated with shorter chronic disease-free life expectancy,[59] and loss of chronic disease-free life expectancy.[60] Workplace bullying at baseline increased risk of CHD or stroke by 59% and by 25% over more than 12 years of follow-up in those who reported physical violence or threat of violence at work after adjustment for confounders.[61]

Reduced life expectancy is likely driven through increased CVD risk factors. Strong evidence links work stress to increased risk of hypertension,[62] insomnia,[63] and negative affectivity.[64] Further, effects can be cumulative.[65] Maladaptive compensatory behaviour patterns (smoking,[66] physical inactivity,[67] self-damaging alcohol consumption, and other unhealthy lifestyle patterns)[68] also drive work-related stress burdens that can result in CVD.[69] Unemployed persons have equally high prevalences of unhealthy lifestyles, biological CV risk factors, and CVD.[70–73] Work stress is therefore an important mediator of CVD risk and outcome. If people with CVD voice concern about work stress, they should be appropriately counselled as suggested in *Section 5*.

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4.4. Socioeconomic and subjective social status

Low socioeconomic status (SES) is an independent risk factor for CVD.[74] Subjective social status (SSS), which refers to the 'individual's perception of his or her own position in the social hierarchy',[75] is also an important mediator of CVD risk. Risk appears to be mediated through lifestyle pathways, however, it is increased via delayed or poor CVD management.[76] Whilst healthcare professionals may be limited in their ability to address these factors, there remains a need to advocate for social policies to address inequalities in SES for those with such a remit.

4.5. Perceived discrimination

Lifetime discrimination (experiences of unfair treatment in various life domains) and everyday discrimination (frequency of day-to-day occurrences of perceived unfair treatment), and related features like social stigmatization, have been linked to CVD.[77] Multiple studies have demonstrated that lifetime discrimination increases CVD risk or all-cause mortality even after adjustment for important confounders.[77–80] The strength of the evidence suggests that discrimination is important, thus people describing discrimination in the clinical setting should be appropriately counselled in terms of prevention of health hazards.

4.6. Mental stress through impaired social relationships

There are multiple avenues through which mental stress can drive CVD risk and prognosis. Important categories of mental stress are summarized below.

4.6.1. Adverse childhood experiences

Adverse childhood experiences (ACEs) are broadly defined as 'childhood events, varying in severity and often chronic, occurring in a child's family or social environment that cause harm or distress, thereby disrupting the child's physical or psychological health and development'.[81] These events include physical, sexual, or emotional abuse, neglect, caregiver mental illness, and domestic violence.[81] Several studies comparing adults with and without ACEs exposure have shown higher incidence of CVD, type 2 diabetes mellitus, depression, and all-cause mortality.[82–86] Healthcare professionals must be aware of the relationship between ACEs and CVD, and if described during clinical interview they should raise awareness to the potential health ramifications and refer these individuals to the appropriate preventative services.

4.6.2. Partnership violence

Intimate partner violence is associated with a greater prevalence of mental health conditions,[87] and appears to be an additional stressor that directly and indirectly impacts women's CV health. However, the findings across studies are inconsistent.[88] Although the evidence is more limited in males, experiences of intimate partner violence, whether as victim or perpetrator, have been linked to increased CVD risk.[89]

4.6.3. Loneliness and social isolation

Loneliness is defined as a 'subjective negative experience that results from inadequate meaningful connections, where "inadequate" refers to the discrepancy or unmet need between an individual's preferred and actual experience'.[90] Social isolation whilst conceptually similar is defined as 'an objective "lack" or "absence" of social contact or relationships'.[91] Evidence from meta-analyses and population-based cohort studies have determined that both loneliness and social isolation are associated with increased CVD risk.[92,93] Healthcare professionals should be aware of the potential impact these experiences have on CVD risk. Social prescribing may be a potential intervention to improve social isolation and loneliness as discussed in *Section 5*.

4.7. Mental health conditions and personality traits as risk factors for cardiovascular disease

4.7.1. Depression

The WHO defines depressive disorder as a common mental condition that involves a low mood or loss of pleasure or interest in activities for long periods of time.[94] Common symptoms are feelings of sadness, emptiness, hopelessness, having trouble concentrating, losing interest in things that one used to enjoy, feeling worthless, guilt, and experiencing disrupted sleep.[94] Depressive mood is a normal reaction to severe adverse life events and problems (i.e. divorce, job loss). Diagnostic criteria for depressive disorders are shown in Supplementary data online, *Table S1*. The prevalence of depression is estimated to be 4.4% in the general population (in total, 322 million globally) posing a significant public health challenge.[94] Depression has been shown to be as strong a CV risk factor as traditional somatic risk factors.[95,96] Large observational and case-control studies demonstrate that depression is independently associated with incident CVD, all-cause mortality, and combined CVD/mortality outcome, with hazard ratios (HRs) or ORs ranging from 1.14 to 1.55.[56,97] Meta-analyses have shown depression to confer increased risk for incident HF, new-onset and recurring atrial fibrillation (AF), ventricular tachycardia/fibrillation, and sudden cardiac death (SCD).[98–101]

4.7.2. Anxiety

Anxiety is an emotion characterized by worrying that may be accompanied by non-specific physical and psychological symptoms such as restlessness, fatigue, difficulty concentrating, irritability, muscle tension, or sleep disturbances.[102] If it is intense and sudden, anxiety may present as a panic attack, with palpitations, shortness of breath, dizziness, chest pain, lightheadedness, or a dying sensation lasting several minutes.[103] Fear and anxiety are closely related phenomena, but differ in terms of their orientation in time. Anxiety is 'future-oriented' (i.e. perceived/anticipated threats), whilst fear is a reaction to a perceived imminent threat in the present.[104]

Anxiety or fear-related disorders are characterized by excessive fear and anxiety that cause distress or impairment in functioning. These disorders include generalized anxiety, panic disorder, agoraphobia, specific phobia, social anxiety disorder, separation anxiety, selective mutism, and other related disorders. Multiple studies and meta-analyses have shown that anxiety and anxiety disorders (together or individually) are associated with increased risk of CVD and/or CV mortality.[105–109] The relationship between anxiety and arrhythmias or HF is less clear with mixed findings.[100,109–111] Panic disorders and panic attacks have also been associated with incident CVD events.[112] Overall, evidence suggests that the link between anxiety or fear and CVD risk is sufficient that healthcare professionals should be aware of the relationship and consider early screening as clinically indicated. Diagnostic criteria for anxiety and fear-related disorders can be found in Supplementary data online, *Table S2*.

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4.7.3. Post-traumatic stress disorder

Post-traumatic stress disorder (PTSD) is a complex and debilitating condition, often stemming from exposure to traumatic events that shatter a person's sense of safety and security.[113] Symptoms encompass intrusive thoughts, flashbacks, nightmares, and heightened arousal, all of which can severely impair an individual's QoL.[114] Onset of PTSD can occur at any time during the lifespan following exposure to a traumatic event.

Post-traumatic stress disorder is an important risk factor for CVD, both in terms of its development and progression. PTSD among Armed Forces veterans has been linked to a 25%–50% higher risk of CVD, including HF, MI, and CVD mortality compared with those without PTSD, even after adjustment for depression and other factors.[115–117] The mechanisms by which PTSD may increase CV risk are not fully understood. However, it has been shown that PTSD elicits psychological, physiological, and behavioural responses that lead to increased risk.[118] Autonomic imbalance (increased activity of the sympathetic nervous system and decreased activity of the parasympathetic nervous system), damaged baroreflex function, and subsequent blood pressure dysregulation may also play a role.[119] PTSD is also associated with elevated markers of inflammation,[120] and often associated with unhealthy diet and lifestyle, obesity, sleep disturbance, decreased physical activity, medication non-adherence, substance abuse, smoking, and alcohol abuse, all of which contribute to poor CV health.[121–123] Definition and characteristics of PTSD can be found in Supplementary data online, *Table S3*. Symptoms and suggested key questions to identify depression, anxiety, or PTSD can be found in Supplementary data online, *Tables S4–S6*.

4.8. Section summary points and management consensus statements from *Section 4*

SECTION SUMMARY POINTS	
(i)	Indicators of positive mental health, such as optimism, happiness, and high life satisfaction are associated with lower CV risk.
(ii)	Hazardous psychosocial factors (e.g. social isolation, financial pressures, and work) are associated with increased risk of developing CVD.
(iii)	Mental health conditions such as depression, anxiety, and PTSD are associated with an increased risk of developing CVD.
(iv)	Healthcare professionals have a responsibility to: • Be informed of these associations. • Be alert to these risk factors during consultation. • Inform, counsel, and refer individuals at risk as needed. • Advocate for system changes as appropriate.
MANAGEMENT CONSENSUS STATEMENTS	
(i)	Management of psychosocial stress and promotion of mental well-being are essential components of integrated CV prevention.
(ii)	Screening for depression, anxiety, and PTSD is advised to be integrated into CV risk assessment.

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5. Mental health and mental health conditions in people with cardiovascular disease

The previous section focused on the analysis of CV risk associated with mental health conditions in individuals without CVD. This section addresses the prevalence of mental health conditions among people with CVD, their impact on CV prognosis, self-management and adherence to medical recommendations, as well as the impact of CVD on the mental health of family members or caregivers.

5.1. Impact of cardiovascular disease on mental health

Cardiovascular disease can induce significant mental health conditions. The perceived characteristics of acute CV events, such as acute coronary syndrome (ACS) or arrhythmia, coupled with the threat of death and helplessness,[124,125] may trigger intense negative emotional responses.[126] Even when diagnostic criteria for mental health disorders are not met, people with CVD may experience existential concerns. These include fear of recurrence, apprehension about death, emotional and work-related stress, anger, grief, and worries about the well-being of family members.[127,128] The need for complex treatment regimens and lifestyle changes negatively impacts QoL and general well-being, and may be difficult to initiate and maintain.[129] Combined with the perceived loss of health and independence, these factors may contribute to an increased risk of developing mental health conditions in people with CVD.

In some instances, these reactions and symptoms might become severe enough to warrant a diagnosis of a mental health disorder, such as depression, anxiety, and even cardiac disease-induced PTSD (CDI-PTSD).[13,125,126] The prevalence of mental health conditions in people with CVD varies widely based on type of CVD, individual characteristics, life contexts, and assessment tools. Most importantly, these comorbid mental health conditions might impact self-management, adherence to medication prescriptions, diet, physical activity, and smoking cessation plans, overall outcomes, and even prognosis in people with CVD.[125,126] This association is particularly evident with stress and depression, where 1 year healthcare costs for society are 33% higher compared with those with CVD.[130] Therefore, it is imperative to inform and educate CV care professionals about the mental health-related consequences of CVD.

5.2. Specific mental health conditions in people with cardiovascular disease: prevalence and prognostic impact

5.2.1. Depressive symptoms and depression

It is important to differentiate depressive symptoms from depression as the term 'depression' encompasses various meanings, spanning from temporary feelings of low mood to severe clinical conditions that are disabling, recurrent, and severe. Moreover, some individuals exhibit a persistently distressed personality with certain depressive traits. People coping with CVD may experience any of these distinct clusters of symptoms, however, the most prevalent type of depression observed following ACS is an 'adjustment disorder with depressed mood'.[131] People meeting the criteria for major depressive disorder are at elevated risk for subsequent events and often experience significantly diminished QoL. Consequently, these individuals require focused efforts for identification, precise diagnosis, and dedicated management.[132]

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Table 1 Prevalence of depression/depressive symptoms in people with cardiovascular disease

CVD	Prevalence data
ACS/Post-MI	Depressive symptoms were reported by 31% of individuals following MI.[136] The prevalence of depression at the time of hospitalization was 40% in women under 60 years, compared with 22% in men of the same age group. Among those over 60 years, the prevalence was 21% in women and 15% in men.[137] In 8580 people with ACS from 22 European countries who were ≥6 months post-hospitalization,[a] depressive symptoms were more frequent in women (32.3%) than men (21.2%), with moderate/severe depression in 12.7% of women and 7.4% of men.[138]
Chronic HF	Clinically significant depression affected 21.5% of people with HF, ranging from 33.6% via questionnaires to 19.3% via interviews, and 11% in NYHA class I to 42% in NYHA class IV.[15] Depression was more common in women with chronic HF (32.7% vs 26.1%), with rates of 11%–67% in women and 7%–63% in men, and increased with higher NYHA functional class.[15]
Advanced HF and post-transplantation	Depression affects 25%–35% of individuals after HTx.[139–141] Depression was reported in 35% of individuals pre-transplant and 26.3% post-transplant.[140] Depression occurs in 15%–39% of people with ventricular assist devices, often exceeding clinical cut-offs, particularly in older people.[114,142] People experiencing HTx had less depression than those with mechanical assist devices.[143]
AF	38% of people with AF met Beck Depression Inventory criteria for significant depression.[144]
ICD	Random-effects meta-analyses showed clinically relevant depression in 15.4% (95% CI 11.9%–18.9%) of people with an ICD at all timepoints post-insertion.[145] The 2 year incidence of new-onset depression after ICD implantation was 11.3% in a national ICD registry.[146] Depressive symptoms affected 20% of people with ICDs (12% mild, 6% moderate, 2% severe). Moderate to severe depression was more common in secondary prophylactic indications and in people experiencing ≥5 ICD shocks.[147] People with ICDs and pacemakers had similarly increased levels of depression.[148]
ACHD	Individuals with ACHD have higher depression rates than the general population, with a weighted prevalence of 24% vs 15%.[149] People with ACHD had a low and comparable suicide risk to the reference cohort.[150]
PH/PAH	In 2161 people with PH, the reported pooled prevalence of depression was 28% (95% CI 20.5–36.8).[134] Smaller studies report depression prevalence in people with PAH ranging from 9% to 70%, linked to disease severity.[151–155]

ACHD, adult congenital heart disease; AF, atrial fibrillation; CI, confidence interval; CVD, cardiovascular disease; HF, heart failure; HTx, heart transplantation; ICD, implantable cardioverter-defibrillator; MI, myocardial infarction; NYHA, New York Heart Association; PAH, pulmonary arterial hypertension; PH, pulmonary hypertension.
[a]This study included: (i) coronary artery bypass graft surgery (including emergency procedures for acute MI), (ii) percutaneous coronary intervention (including emergency procedures for acute MI), (iii) acute MI (ST-elevation and non-ST-elevation MI), and (iv) acute myocardial ischaemia without infarction (troponin-negative).

5.2.1.1. Prevalence of depressive symptoms and depression in people with cardiovascular disease

Depression is one of the most common mental health conditions in people with CVD. The global prevalence of depression among people with CVD, as measured by various self-report questionnaires, is estimated to be 18%.[14] It is more common among women and in older ages, yet healthy and physically functioning older adults are at lower risk of depression compared with young adults.[14,133,134] Depression is associated with several negative lifestyle factors, such as smoking, alcohol intake, physical inactivity, and unhealthy diet, as well as other CVD risk factors including diabetes and hypertension.[135] These potentially modifiable risk factors are all associated with coronary artery disease (CAD), MI, HF, stroke, and mortality.[54] *Table 1* presents examples of studies demonstrating how rates of depression vary based on the condition, diagnostic methods, and population demographics.

5.2.1.2. Impact of depressive symptoms and depression on cardiovascular disease prognosis

Depression is a known risk factor for poor prognosis among people with CVD. While one study did not find a significant impact of depression on CV or all-cause mortality after MI,[156] more recent studies suggest otherwise. For example, post-MI depression, though attenuated by severity, independently predicts a 22% higher all-cause mortality and 13% more CV events per standard deviation increase in depression z-score.[157] Depression has been associated with an increased risk of non-fatal CV events, as well as all-cause mortality after ACS.[17] Even 10 years after percutaneous coronary intervention (PCI) (~50% elective), depression was associated with an increased risk for all-cause mortality.[158] Depression is also a marker of poor prognosis in people with HF, where both depressive symptoms and depressive disorders have been prospectively linked to frequent hospitalizations, recurrent CV events, and mortality.[18] The prospective associations between elevated depressive symptoms or a depressive disorder and HF was associated with a two-fold increased risk of death or CV events.[15] Depression at the start of exercise-based cardiac rehabilitation (ECR) was significantly associated with lower improvement in exercise capacity and QoL during rehabilitation.[129] Depression and previous suicide attempts detected before or after heart transplantation (HTx) may impact long-term HTx outcomes (rejection, cardiac allograft vasculopathy, and death),[159] probably related to increased non-adherence to medications.[160]

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Depression is also related to increased adverse events in people with ventricular assist devices (VAD),[161,162] and is a factor for negative outcomes among people coping with AF. In a meta-analysis consisting of seven cohort studies with 1070 AF people who underwent catheter ablation, depression before the procedure was independently associated with an increased risk of AF recurrence after ablation.[163] Further, symptoms of depression were the strongest independent predictor of future QoL post-ablation.[144]

5.2.1.3. Impact of depressive symptoms/depression on self-management and adherence

One possible path by which depression is associated with adverse outcomes among people with CVD is limited engagement in self-care practices and lack of adherence, as depression is associated with challenges in self-management of CV medication, healthy lifestyle, ECR, and self-care.[129,164–166] Kronish *et al.* reported that people with persistent depression were only half as likely to enrol in an ECR programme compared with those without persistent depression.[167] People with persistent depression also showed lower rates of adherence to smoking cessation, taking medications, and exercising. A recent daily diary study demonstrated that on days when people attending ECR experienced elevated depression symptoms, they engaged in less physical activity and more sedentary behaviour.[168] In a cohort study of individuals who underwent PCI ($n = 124\,443$), participants with depression were 10% to 20% less likely to attain optimal adherence to Guideline-recommended medications compared with those without depression.[169] Finally, a systematic review of quantitative studies indicated that even mild to moderate levels of depression were significantly associated with medication adherence in people with HF.[170]

5.2.2. Anxiety

5.2.2.1. Prevalence of anxiety in people with cardiovascular disease

Systematic reviews and meta-analyses have found prevalence of anxiety among people with CVD to range from 28.9% to 32.9%.[16,171] Higher rates are found using questionnaires (34.8% to 9%) compared with clinical diagnostic interviews (17%). The highest rates of anxiety disorder based on diagnostic interviews were reported in people with undifferentiated chest pain or palpitations (19%). Anxiety tended to be more prevalent among females compared with males (43% vs 29.5%).[171] As with depression, prevalence of anxiety varies by CV condition, method of diagnosis, and population demographics. *Table 2* presents examples of studies demonstrating how rates of anxiety vary based on the condition, diagnostic methods, and population demographics.

5.2.2.2. Impact of anxiety on cardiovascular disease prognosis

A meta-analysis estimating the effect of anxiety on CV outcomes in more than 30 000 people with CAD found that the impact depends on the timing, with no effect of anxiety in the first 2 months after ACS but with a negative effect on outcome in people with stable CAD.[19] Generalized anxiety disorder, present in 5.5% of people 3 months after acute MI (AMI), was associated with a two-fold increased risk of adverse outcomes (CV events and all-cause mortality) during a 10 year follow-up period.[184] There is little effect of anxiety symptoms alone on outcome in HF although comorbid anxiety and depression increase the risk for rehospitalization and mortality in people with HF.[185–187] Among people with an implantable cardioverter-defibrillator (ICD), anxiety was a strong predictor of mortality with an OR of 4.17 in a cross-sectional national survey in Denmark.[188]

5.2.2.3. Impact of anxiety on self-management and adherence

Interestingly, anxiety, as opposed to depression, may encourage people to be adherent (e.g. to their medication regimen) and can have a positive impact on clinical outcome in people with CVD.[189,190] However, anxiety disorders are mostly linked with unhealthy lifestyle, poor adherence to lifestyle modification, and lower participation in ECR.[138] One possible explanation of this trend is people with anxiety have a tendency to avoid reminders of the illness.[191]

5.2.3. Cardiac disease-induced post-traumatic stress disorder/symptoms

5.2.3.1. Prevalence of post-traumatic stress disorder in cardiovascular disease

Cardiac disease-induced PTSD, or post-traumatic stress symptoms (PTSS) defined as post-traumatic symptoms to full disorder emerging from an acute CV event or intervention, has a heterogeneous incidence among different types of CVD. *Table 3* presents examples of studies demonstrating how rates of PTSD and PTSS vary based on the condition, diagnostic methods, and population demographics.

5.2.3.2. Impact of post-traumatic stress disorder on cardiovascular disease prognosis

Cardiac disease-induced PTSS are linked to numerous adverse physical and emotional outcomes, including increased overall psychopathology and heightened mortality risk. However, due to the predominantly cross-sectional or retrospective nature of existing studies, distinguishing the effects of CDI-PTSS from those of the triggering event remains challenging. Nevertheless, the association between CDI-PTSS and elevated rates of mortality and CV events underscores the need for further research.[13]

Studies examining the implications of CDI-PTSS on subsequent MACE or all-cause mortality yielded mixed results. The severity of intrusion symptoms (intrusive thoughts or images related to the traumatic event, nightmares, and flashbacks) measured 1 month after a first MI predicted recurrent MACE/all-cause mortality 42 months later.[198] People scoring >11 on the intrusions dimension of the Impact of Event Scale (IES)[199] had a three times higher risk of developing MACE and all-cause mortality than did those classified as low on this symptom cluster.[198] Similarly, dissociative symptoms during hospitalization predict 15 year all-cause mortality among people with MI,[200] and people with above-threshold PTSD-related symptoms at 6 months post-event had a 42%–50% prevalence of experiencing other serious CV events during the next 6 months compared with a 26%–32% prevalence of the same among people without PTSS.[201] Other studies found that PTSD measured 4 to 6 weeks post-MI was not predictive of MACE 9 months later.[202]

Cardiac disease-induced PTSS predict non-fatal CVD-related hospital readmissions 1 to 4 years after a previous index MI.[203] Increasing levels of CDI-PTSS, measured by the IES and PTSD Symptom Scale,[204] are associated with CV readmissions.[205] Further, people with IES-reported PTSS

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Table 2 Prevalence of anxiety/anxiety symptoms in people with cardiovascular disease

CVD	Prevalence data
ACS/Post-MI	In an international cohort of people with CABG, PCI, post-MI, and ACS ≥6 months post-hospitalization, anxiety prevalence ranged from 12% to 42% in men and 22% to 64% in women, with moderate to severe anxiety[a] in 11% of men and 23% of women.[138] At 3 months post-MI, 10% reported high anxiety, dropping to reference population levels[b] at 3–18 months.[172] In people diagnosed with SCAD, 41% had mild anxiety and 16% moderate to severe anxiety by questionnaire. Higher anxiety scores were more common in women, younger individuals, those with lower resilience, and those closer to the event.[173]
Chronic HF	Up to 72% of people with HF experience anxiety, with pooled estimates of 56% for symptoms, 29% for clinically significant anxiety, and 13.1% for anxiety disorders. Prevalence was higher in studies with more female participants.[174] People with HF face a higher risk of anxiety, with 23% experiencing symptoms and 32% having both anxiety and depression.[175]
Advanced HF and post-transplantation	The pooled prevalence of anxiety among people experiencing HTx was 11% (95% CI 3.8%–28.5%).[176]
AF	People with AF exhibited a 28% prevalence of anxiety at baseline, comparable to controls, with symptoms persisting in 37% after 6 months.[144] Among people undergoing cardioversion or ablation, 30% reported clinically significant anxiety.[177]
ICD	Among OHCA survivors, anxiety was reported in 36% of women vs 20% of men, with higher rates in younger women (<55 years) than older women (43% vs 28%).[178] At 18 months post-OHCA, 32% showed anxiety symptoms.[179] A large-scale registry reported 20% anxiety among people experiencing OHCA.[180] Random-effects meta-analysis found clinically relevant anxiety in 23% (95% CI 18.3%–27.0%) of people with an ICD at all timepoints post-insertion.[145] New-onset anxiety incidence was 15% at 24 months post-ICD implantation, with higher rates in women and the secondary prevention setting.[146,181] People with ICDs and pacemakers exhibited similarly elevated anxiety levels.[148]
ACHD	A review found anxiety symptoms to be common both immediately after CV events or surgery and during follow-up.[182] Anxiety prevalence was higher in people with ACHD (13%) compared with a historical cohort of people with non-Hodgkin lymphoma and German reference values (6%).[183]
PH/PAH	A total of 24 studies with 2161 people with PH reported a pooled prevalence of 37% for anxiety (95% CI 28.7–46.4).[134] Smaller studies reported anxiety prevalence in people with PAH ranging from 9% to 58%, linked to disease severity.[151–154] Anxiety incidence was higher in people with PAH living in urban areas and in non-smokers or non-drinkers compared with their counterparts.[154]

ACHD, adult congenital heart disease; ACS, acute coronary syndrome; AF, atrial fibrillation; CABG, coronary artery bypass graft; CI, confidence interval; CV, cardiovascular; CVD, cardiovascular disease; HADS, Hospital Anxiety and Depression Scale; HF, heart failure; ICD, implantable cardioverter-defibrillator; MI, myocardial infarction; OHCA, out-of-hospital cardiac arrest; PAH, pulmonary arterial hypertension; PCI, percutaneous coronary intervention; PH, pulmonary hypertension; SCAD, spontaneous coronary artery dissection.
[a]HADS anxiety score ≥8.
[b]Norwegian population.

are more than twice as likely as those without PTSS to be readmitted during the year following their MI.[206] However, other studies showed that PTSD measured by the Post-traumatic Diagnostic Scale may not be associated with frequency of CVD-related hospital readmissions.[207]

5.2.3.3. Impact of post-traumatic stress disorder on self-management and *adherence to medical recommendations*

Evidence on CDI-PTSD and non-adherence is mixed, with some studies showing positive associations and others not.[201,206,208–210] However, stronger evidence links CDI-PTSD to non-adherence to medication and physical activity.

5.2.4. Loneliness and living conditions

In a cross-sectional study of hospitalized people with various types of CVD, loneliness measured at discharge was associated with significantly worse outcomes in men and women.[211] Moreover, loneliness predicted all-cause mortality risk, which was almost three-fold among women and two-fold among men. Living alone predicted CV event risk in men only (HR 1.39; 95% CI 1.05–1.85).[211] In a prospective randomized controlled trial (RCT) in people with stable CHD, living alone was related to a higher risk of CV death and the primary composite endpoint of non-fatal MI or non-fatal stroke. Being married, as compared with being widowed, was associated with a lower risk of CV death and the primary composite endpoint.[212]

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Table 3 Prevalence of post-traumatic stress disorder/post-traumatic stress symptoms in people with cardiovascular disease

CVD	Prevalence data
ACS/Post-MI	Clinically significant PTSD 12%, and PTSS prevalence 0%–26% depending on type of measurement.[13,192] PTSD occurs in 7%–20% of people post-CABG.[13] PTSD prevalence among people with SCAD ranged from 28% to 35%.[173,193]
Advanced HF and post-transplantation	PTSD occurs in 11%–19% of people post-HTx.[13]
ICD	12%–38% prevalence of PTSD in survivors of cardiac arrest.[13,145,178] Experiencing ≥1 appropriate ICD shocks was an independent risk factor for PTSD (OR 6.0; 95% CI 1.45–24.63; $P < 0.013$).[194] A single study found higher PTSD prevalence in people with ICD who experienced electric storms compared with those who did not.[195]
ACHD	1%–30% prevalence of PTSD in people with ACHD, varying by measurement and geographical region.[196,197] Women and people with multiple medical encounters lacking psychosocial intervention are more likely to have PTSD.[196]

ACHD, adult congenital heart disease; ACS, acute coronary syndrome; CABG, coronary artery bypass graft; CI, confidence interval; CVD, cardiovascular disease; HF, heart failure; HTx, heart transplantation; ICD, implantable cardioverter-defibrillator; MI, myocardial infarction; OR, odds ratio; PTSD, post-traumatic stress disorder; PTSS, post-traumatic stress symptom; SCAD, spontaneous coronary artery dissection.

5.2.5. Chronic stress

Chronic stress, defined as the experience of physical and emotional imbalance determined by life events and conditions, was found in 58% of people with CVD based on a systematic review (five studies, $n = 533$).[16] A large observational study ($n = 3572$) reported that perceived stress was significantly higher in women vs men at baseline and 1 month after MI.[213] Perceived chronic stress was associated with worse recovery in overall QoL and mental status among people with MI.[213]

Recent studies have focused on the concept of CV distress, defined as '*a persistent negative emotional state rather than a transient state; involving multiple psychosocial domains; that challenges a person's capacity to cope with living with their heart condition, the treatment of the condition, and the resultant changes to daily living; and challenges the person's sense of self and future orientation*'.[214] This study, using the Cardiac Distress Inventory-Short Form (CDI-SF), found significantly higher scores on the CDI-SF among younger people and women.[214] People with HF and elevated stress levels may undergo a more challenging disease trajectory, characterized by a diminished QoL and heightened susceptibility to adverse events.[215] Indeed, people with HF reporting high stress levels had a higher likelihood of adverse events during the study period.[216]

5.3. Addressing the mental health needs of informal caregivers for people with cardiovascular disease

Following the initial diagnosis, people may be asked to implement substantial lifestyle changes to reduce CV risk, prevent further disease progression, and enhance QoL.[217] Coping with CVD and embracing new habits can prove challenging, and for adults, the primary source of support often comes from their informal caregivers, primarily their partners.[218,219] Partners are usually the most available and accessible persons for support, physically during hospitalizations and medical visits, at home, and emotionally.[220]

The caregiving efforts of informal caregivers can exert a significant toll on themselves.[31,35] Providing emotional and tangible support to a person coping with CVD may lead to caregiver emotional and/or physical strain. Some studies have identified mental health risks, such as increased levels of anxiety, depression, or CDI-PTSD among caregivers in the context of CVD.[31–33,220] A recent review[221] suggested that low to moderate levels of distress were common among family caregivers of people with CAD (prevalence ranging from 6% to 67% of caregivers). Family caregivers of people with HF cope with significantly higher physical and psychological health risks compared with non-caregivers.[222] In the context of a VAD implantation, spouses have been found to have higher anxiety rates compared with the person with the VAD,[223] as well as lower mental QoL as a consequence of VAD-related disturbances in sexual activity.[224]

Despite ample literature documenting the adverse effects of caregiving, the person with CVD is seen as the sole focal point of attention and exclusive recipient of care, thus overlooking the needs of the informal caregiver.[34] A shift in healthcare systems from focusing solely on individuals to adopting a holistic approach that includes the individual and their families, is needed. Family caregivers are essential collaborators, as they often ensure people can build change into their lives and adhere to their treatment plans. Educating and supporting informal caregivers represents not only a mechanism for improving long-term outcomes, but also a means of reducing healthcare costs through the avoidance of repeat engagements with the health system.[225,226] Most importantly, caring for informal caregivers not only benefits the person living with CVD and reduces medical costs, but also reflects a holistic approach to CV practice. By supporting informal caregivers, a compassionate and sustainable healthcare system of CVD management is fostered, which is essential for the long-term success. Different Psycho-Cardio team members engage with informal caregivers at varying levels. Every team member should remain mindful of the challenges faced by those who care for a person living with CVD. *Figure 6* outlines specific actions the Psycho-Cardio team members can take to assess and alleviate caregiver distress.

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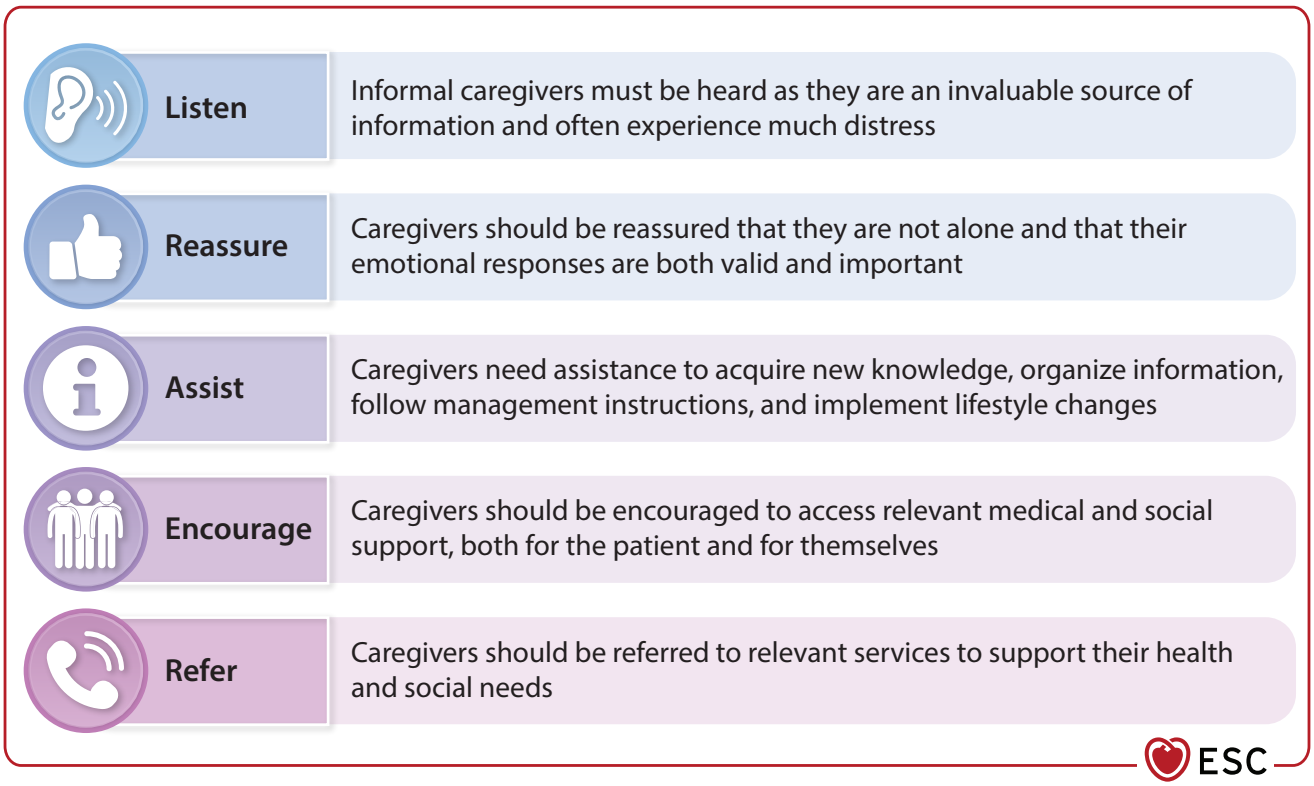
Listen
Informal caregivers must be heard as they are an invaluable source of information and often experience much distress
Reassure
Caregivers should be reassured that they are not alone and that their emotional responses are both valid and important
Assist
Caregivers need assistance to acquire new knowledge, organize information, follow management instructions, and implement lifestyle changes
Encourage
Caregivers should be encouraged to access relevant medical and social support, both for the patient and for themselves
Refer
Caregivers should be referred to relevant services to support their health and social needs
ESC

Figure 6 Suggestions for supporting informal caregivers of people living with cardiovascular disease.

5.4. Section summary points and management consensus statements from *Section 5*

SECTION SUMMARY POINTS	
(i)	There is a multidirectional association between CVD and mental health conditions such as depression, anxiety, and PTSD, increasing each other's risk.
(ii)	Mental health conditions in people with CVD, such as depression, can negatively affect self-management, including adherence to medication and lifestyle changes, and are associated with worse outcomes.
(iii)	The effects of anxiety and PTSD on adherence and CV outcomes are less clear and might be time-dependent.
(iv)	Caregivers play an essential role in supporting their family members who cope with CVD to incorporate lasting lifestyle changes and to adhere to treatment plans: assessing and supporting caregivers well-being benefits both parties.
MANAGEMENT CONSENSUS STATEMENTS	
(i)	It is reasonable to assess depression, anxiety, and PTSD in people with established CVD as they are highly prevalent and impact outcomes, and refer promptly to a professional when needed.
(ii)	Chronic stress and loneliness are associated with negative outcomes in people with CVD and should prompt referral if identified during clinical assessment.
(iii)	Incorporating informal caregiver well-being assessment and support is advisable in the holistic approach of mental and CV health.

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6. Identification, prevention, and management of mental health issues in people with cardiovascular disease

6.1. Awareness of needs in people with cardiovascular disease

Depression and anxiety can easily be overlooked in the routine care of people with CVD and/or considered 'normal' reactions to the clinical and prognostic burden of their disease. Given the high prevalence of mental health conditions among people with CVD, and their impact on outcomes and adherence, the possibility of evaluating mental health status at some point during professional encounters can be considered a worthy strategy to improve health. People with CVD with potential symptoms of mental health conditions should undergo formal screening and, at least, a low threshold for formal screening of mental health symptoms should be applied in people with CVD.

The recent manuscript '*How your patient is really feeling: the emotional hinterland of a cardiac diagnosis*', written by individuals with CVD, illuminates their experience.[30] In this piece, people coping with CVD highlight challenges faced when diagnosed, gaps in care, and unmet needs.[30] Priorities, such as the need for an on demand, accessible, tailored, and long-term multidisciplinary support network, are outlined. Suggestions for establishing the best possible person-centred support system and components for long-term support are outlined in *Figure 7*. Additional experiences of people coping with CVD, presented in the associated 'Clinical cases and patient perspectives' text, further highlight the importance of integrating mental health assessment within CVD care.

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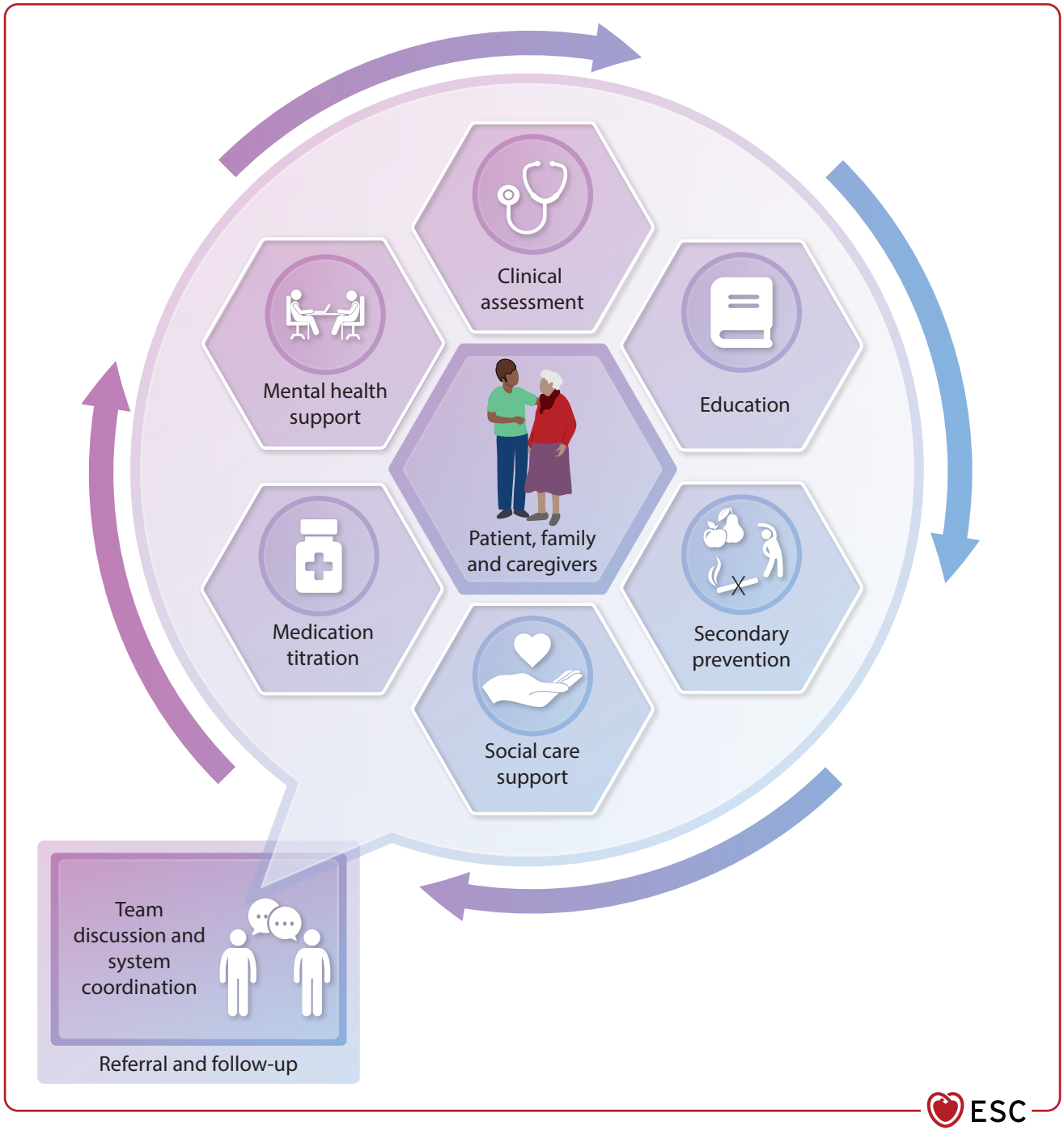

Figure 7 Visualization of an 'on demand' support system for people with cardiovascular disease to improve mental health. Cardiovascular disease support team on standby. People with cardiovascular disease, family members and caregivers access the relevant healthcare or allied professional, or other resources appropriate to their immediate need, the process is cyclical, allowing for repeat access as needed. Adapted from Mindham *et al.* with permission[30].

6.2. Identification and screening

Taking a clinical history is an opportunity for the evaluation of potential symptoms and any history of mental health conditions. Conversations during the clinical course are further opportunities to identify previously unrecognized symptoms, the appearance of new difficulties, manifestations of mental health conditions, or the need for help. These may indicate a requirement for more education relating to their condition(s) or support from social care services, which is not unusual in people with CVD.[227]

To ensure that people are being screened and treated for potential mental health conditions in addition to their underlying CVD, consideration needs to be given to: (i) who will screen, (ii) when screening should be performed, (iii) which screening tools should be used, and (iv) how often screening should occur (*Figure 8*). Given that resources may vary across countries, hospitals, and specialized and general practices, a one-size-fits-all approach is unlikely to work. Collaboration with mental health professionals (the Psycho-Cardio team) can support developing a protocol for screening and guiding referrals based on severity

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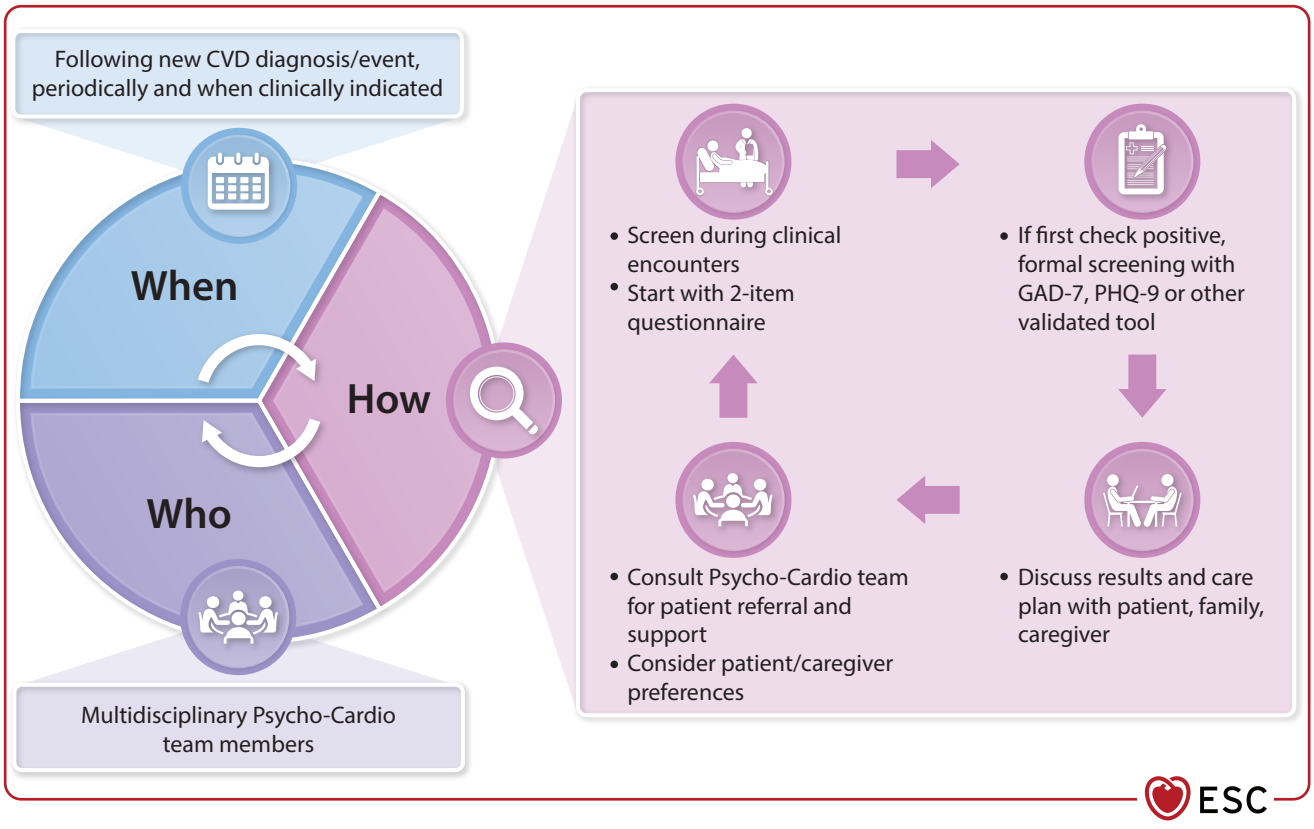
Following new CVD diagnosis/event, periodically and when clinically indicated
When
How
Who
Multidisciplinary Psycho-Cardio team members
• Screen during clinical encounters
• Start with 2-item questionnaire
• If first check positive, formal screening with GAD-7, PHQ-9 or other validated tool
• Discuss results and care plan with patient, family, caregiver
• Consult Psycho-Cardio team for patient referral and support
• Consider patient/caregiver preferences
ESC

Figure 8 Screening for mental health conditions in people with cardiovascular disease. CVD, cardiovascular disease; GAD, Generalized Anxiety Disorder; PHQ, Patient Health Questionnaire.

of mental health conditions and local situation. Ideally, screening for anxiety and depression should be conducted following a new diagnosis of CVD or acute CV event, at least once during follow-up and periodically (e.g. annually or when clinically indicated). Brief two-item screening measures ensure that the time needed for initial screening is limited (see *Section 5.2.1*).

- *When should the screening be done?* Following a new diagnosis of CVD or acute CV event, periodically, at least once during follow-up, or when clinically indicated.
- *How should screening be done?* Via use of any valid and reliable short screening tool, appropriate to the setting and context.
- *Who should screen?* Any member of the Psycho-Cardio multidisciplinary team who are appropriately qualified to do so.

Of note, screening by itself does not help people with CVD but includes responsibility to address and provide appropriate referral and treatment options. Further, it is important to acknowledge that screening has been linked to psychological harms (worry and anxiety) that remain underexplored in the context of CVD.[228] A proposal for the who, when, and how of screening for mental health conditions in people with CVD is illustrated in *Figure 8*.

6.2.1. Assessment of depression and anxiety

Two-item screening tools, which only take a few minutes to answer, are the simplest way to assess depression and anxiety. We highlight three measures, the Whooley questions, the Patient Health Questionnaire (PHQ)-2, and the Generalized Anxiety Disorder (GAD)-2. Positive screens indicate the need for a longer screening measure. The Whooley questions are a two-item screening tool for the identification of depression that has shown high sensitivity and moderate specificity,[229] making this measure a useful initial screening tool for depression:[32,230–233]

The Whooley questions[229]

(i) During the past month, have you often been bothered by feeling down, depressed, or hopeless?

(ii) During the past month, have you often been bothered by little interest or pleasure in doing things?

'Yes' to one (or both) questions = positive test (requires further evaluation).

'No' to both questions = negative test (not depressed).

The two-item and seven-item GAD questionnaires, and the two-item and nine-item PHQ tools for depression are widely used with good sensitivity and specificity in people with CVD.[234–237] The GAD and PHQ have been translated into many languages and their use does not require a license agreement. Their psychometric properties are shown in *Table 4*.

Although it can be a challenging task to choose a screening tool, generic questionnaires are widely used. It is key to find a screening tool that is valid and reliable for people with CVD. The Hospital Anxiety and Depression Scale (HADS) is widely used, including in people with CVD in the inpatient and outpatient setting. However, use of the HADS requires a license fee. The joint ESC societies statement on patient-reported outcome measures, referred to in *Section 5.1.1*,[239] also notes the Cardiac Anxiety Questionnaire, Cardiac Depression Scale, and Cardiac Distress Inventory can be considered as possible measures.

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Table 4 Psychometric properties of screening tools for anxiety and depression symptoms

Psychometric property	Whooley questions[a]	GAD-2[b]	PHQ-2[b] ≥2 points
Sensitivity	95% (95% CI 88–97)	91%	97%
Specificity	65% (95% CI 56–74)	37%	48%

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CI, confidence interval; GAD, Generalized Anxiety Disorder; PHQ, Patient Health Questionnaire.
[a]Validated in an unrestricted population, i.e. not specifically CVD.[232]
[b]Validated in an Australian population.[238]

Table 5 Timing and tools for screening anxiety and depression symptoms

Timing of screening	Measurement	
	Anxiety symptoms	Depressive symptoms
(1) Following a new diagnosis of CVD, a CV event or procedure. May be during hospitalization. (2) At follow-up (e.g. annually) to determine change from baseline or previous measurement (3) Anytime based on clinical judgement	GAD-2 followed by GAD-7 if positive	PHQ-2 followed by PHQ-9 if positive

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CV, cardiovascular; CVD, cardiovascular disease; GAD, Generalized Anxiety Disorder; PHQ, Patient Health Questionnaire.

Mental health conditions can evolve over time and may be episodic. Therefore, professionals involved in the long-term management of people with CVD need to be aware of their mental well-being, and its changes so, ideally, its assessment should be seamlessly integrated into routine care (*Table 5*). Supplementary data online, *Tables S4–S6* offer examples of targeted questions that might be helpful to address specific aspects of depression, anxiety, and PTSD during clinical encounters.

The intensity of symptoms may also change over time. A recent study of people without distress at the time of ICD implant found that 14.5% developed new-onset anxiety and 11.3% new-onset depression during 24 months of follow-up.[146] One cue that might be helpful is to monitor scores at the time of first screening (e.g. when being implanted with the ICD), as people with a high score at that time are more likely to also have an increased score at follow-up.[240]

The value of routine screening is still debated, therefore robust mandates have been avoided. The Comparison of Depression Interventions After Acute Coronary Syndrome: Quality of Life (CODIACS-QoL) RCT is one of few studies where screening for depression within 2–12 months post-ACS with or without providing depression treatment, did not alter quality-adjusted life years, depression-free days, or led to harm.[235] Nonetheless, European and American Guidelines recommend assessment and screening for depression and anxiety (usually during hospitalization), although do not specify how often.[132,241–244] Therefore, the optimal timing of screening within different CV conditions is not established. This Task Force considers it prudent to screen people after a new diagnosis of CVD or a CV event, then periodically (e.g. annually and at least once during follow-up), and when clinical judgement indicates that it is needed (*Table 5*). Screening can be conducted during hospitalization if time permits.

6.2.2. Suggested approach to screening people with cardiovascular disease for psychological distress, depression, and anxiety

There are two ways in which people can be assessed: (i) by means of a clinical diagnostic interview, or (ii) screening by a questionnaire that can identify symptom levels but not deliver a diagnosis.

In clinical practice the diagnostic interview may be lengthy, requires specific expertise, and thus is likely untenable to perform as a routine practice in most clinical settings. However, given that elevated scores on a screening questionnaire as well as a diagnosis of depression or anxiety increases the risk of morbidity, mortality, and poor QoL, questionnaires are a reasonable starting point. High scores on a screening instrument should lead to referral to a mental health professional for assessment and/or diagnosis. Questionnaires also provide the means for monitoring changes in symptoms over time. As noted previously, there are several options with respect to questionnaires to choose from and it is important to know the reliability, validity, and appropriate usage of the instruments.

6.2.3. Challenges in specific cardiovascular conditions

In people with HF, depression and anxiety can easily be overlooked in routine care due to overlapping symptoms, such as fatigue, apathy, lack of energy, and sleep disorders. Thus, there is a risk that both people with HF and healthcare professionals may misinterpret the situation. Depression and anxiety can also be considered 'normal' reactions to the clinical and prognostic burden of HF. Although routine screening for mental health conditions using validated questionnaires and tools is advised during hospitalization and follow-up,[29,241] it is still not clear when and where to screen people with HF. The diagnosis of mental health conditions can also be affected by the continuous fluctuations of HF symptoms that can interfere with mood and psychology.[241,245,246]

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Psychosocial assessment is an essential component of the evaluation of candidates for VAD, mainly aimed at identifying targets for treatment and improvement before the procedure, but also identifying potential contraindication in some candidates (e.g. uncontrolled psychiatric conditions, consistent non-adherence, active substance abuse). A consensus document on psychosocial assessment in advanced HF,[247] endorsed by multiple societies, defined the main domains to evaluate as:

- Risk factors for poor post-HTx or VAD outcomes.
- Capacity to engage in decision-making.
- Personal and environmental resources.
- Capacity to operate VAD.

Two scores have been used for psychosocial assessment in HTx: the Psychosocial Assessment of Candidates for Transplantation (PACT) and the Stanford Integrated Psychosocial Assessment for Transplantation (SIPAT). Both have shown good predictive capacity to identify people at risk of post-HTx non-adherence and psychosocial complications,[248,249] although their impact on clinical outcomes is unclear. These tools have not been validated in the VAD population.

Quality of life and mental health assessment are needed in people with pulmonary hypertension (PH) due to the high reported prevalence of depression and anxiety (see *Section 5*, *Tables 1* and *2*), but there is lack of evidence on the ideal timing or specific method. The HADS may be a useful tool, since it was able to rule out anxiety and depression disorder with a negative predictive value of 90% in a PH population.[250]

6.2.4. Assessment of subjective well-being and quality of life

The WHO-5 questionnaire, available in 30 languages,[251,252] can be used to assess SWB and does not require a license fee. A percentage score <50 (or a raw score <13) has been suggested as a cut-off for poor mental well-being and as an indication for further assessment for the possible presence of a mental health condition (e.g. depressive disorder).

Patient-reported measures such as QoL are seen as essential in clinical practice as well as in clinical trials as ways to assess symptoms, function, well-being, perspectives, and undisclosed problems. Several disease-specific QoL instruments are available, valid in specific conditions such as HF, ischaemic heart disease (IHD), AF, congenital heart disease, and PH. Generic measures such as the Short-Form 12 or 36 or EuroQol 5-Dimension (EQ-5D) questionnaire are often used as well. Most QoL instruments include items related to mental health status as well as physical health, which can alert a healthcare professional to a need for screening for mental health conditions. These instruments are being incorporated into electronic medical records in some systems, but implementation of regular QoL assessment is hindered by limited integration into clinical practice and interpretation of scores. However, electronic medical records and automated systems should in future simplify assessment of well-being, QoL, and mental health conditions at regular intervals. A full list of these measures can be found in a recent ESC statement on 'Placing patient-reported outcomes at the centre of CV clinical practice'.[239]

6.3. Management of mental health conditions in people with cardiovascular disease

Given the negative impact of poorer mental health on adherence to medication and lifestyle, QoL, prognosis, and costs, people with an increased symptom score on anxiety and/or depression questionnaires and those with a diagnosis of anxiety disorder, depression, or PTSD, should be considered potential candidates for receiving treatment. Although evidence is sparse that people with CVD screened for anxiety and depression and treated afterwards have a better prognosis,[235] there are a few promising studies. A retrospective cohort study of people with depression who received psychotherapies via primary care services ($n = 636\,955$), reported that intervention-driven improvements in depression symptoms were associated with a lower risk of any-cause new-onset CVD (HR 0.88; 95% CI 0.86–0.89). Subanalyses suggested the association was greater in those <60 years of age.[253] In recognition of the different levels of stress, anxiety, depression, and PTSD experienced, and therefore the different needs with respect to treatment, a stepped care approach (*Figure 9*) would be one way forward.[254–257] Stepped care takes into account people's preferences and can be adapted to symptom severity and resources available, and does not mean that all earlier steps need to be done before accessing higher level support.

6.3.1. Communication, education, and support for people with mental health conditions and cardiovascular disease

Effective communication is a cornerstone of healthcare delivery, fostering person-centred care, and addressing the complex interplay between mental and physical health.[258] Proportional stress, anxiety, or fear may be normal reactions after a diagnosis of CVD, acute CV events, CV procedures or interventions, or their complications. Empathy and active listening are essential to understanding the potential difficulties and worries the person with CVD and their family members may face. It is important to recognize that challenges may not only be due to the physical consequences of CVD or its therapy. Rather, healthcare professionals must appreciate the full spectrum of mental and emotional consequences, as well as the impacts this may have on lifestyle, professional, family, social, or economic factors as presented in the associated 'Clinical cases and patient perspectives' document. Healthcare professionals should ensure that people receive support for both physical and mental health needs, preventing or attenuating unwanted psychological or emotional reactions, and potentially improving therapeutic adherence and clinical outcomes.[259]

Open dialogue with people with CVD, family, and caregivers, adapted to their age, cultural level, beliefs, and preferences, is essential.[260] Answering questions, solving doubts and clarifying uncertainties is a key aspect of therapeutic relationships and may help prevent misunderstandings and irrational fears.[261] While in ECR programmes there is more time and opportunity for communication, this may be challenging to deliver in acute or critical care and in outpatient care, where time pressure is constant. In these settings, time for high-quality communication should be facilitated.

Multiple individual, professional, condition-specific, and organizational factors including health literacy, mental health issues, and time pressures, impact the quality of communication. The impact of mental health on communication may be particularly strong in people with SMI. Shared decision-making (SDM), in which the person coping with CVD and professionals discuss evidence and options for treatment, and people are supported to make informed decisions, is dependent on good communication. A systematic review and meta-analysis of interventions to increase SDM in CVD found that the interventions reduced decisional conflict and increased knowledge across a wide range of CVD conditions and formats.[262]

Compassion in CVD care is an important element in communication and understanding. More information on compassionate care can be

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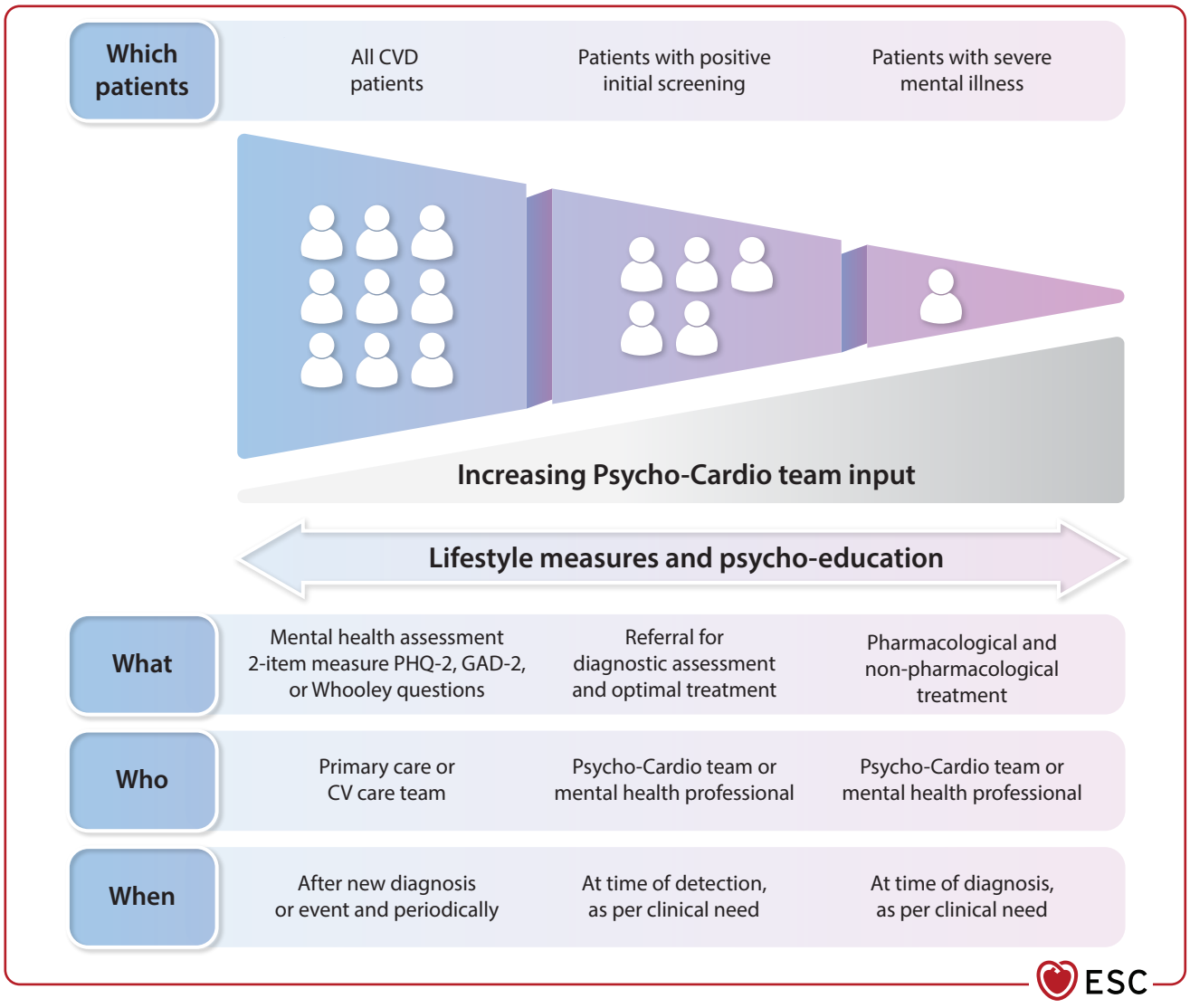
Which patients
All CVD patients
Patients with positive initial screening
Patients with severe mental illness
Increasing Psycho-Cardio team input
Lifestyle measures and psycho-education
What
Mental health assessment 2-item measure PHQ-2, GAD-2, or Whooley questions
Referral for diagnostic assessment and optimal treatment
Pharmacological and non-pharmacological treatment
Who
Primary care or CV care team
Psycho-Cardio team or mental health professional
Psycho-Cardio team or mental health professional
When
After new diagnosis or event and periodically
At time of detection, as per clinical need
At time of diagnosis, as per clinical need
ESC

Figure 9 Stepped care model for assessment and management of mental health conditions in people with cardiovascular disease. CV, cardiovascular; CVD, cardiovascular disease; GAD, Generalized Anxiety Disorder; PHQ, Patient Health Questionnaire. Adapted from Pedersen *et al* with permission.[254]

found in supplementary data online, and *Table S7*. Caregivers and family involvement can improve mental well-being and CV outcomes; a paradigm shift in the organization of care may be needed to include the person's social environment into treatment. More information can be found in the supplementary data online.

6.3.2. Psychological interventions

A broad range of strategies, from cognitive-behavioural therapy (CBT), psycho-education, and mindfulness-based techniques to lifestyle modification programmes and support groups, including internet-based interventions and mobile health (mHealth) solutions, have been proposed as psychological therapeutic options for people with CVD.[263]

6.3.3. Psycho-education

Psycho-education is an intervention with structured knowledge transfer about an illness and its treatment, integrating emotional and motivational aspects to enable people to cope with the illness and to improve its treatment adherence and effectiveness.[264] It is considered an important component of treatment in both medical and mental health conditions.[265] A psycho-educational approach is already embedded within multiple CV care settings, including ECR and secondary prevention programmes. It includes education on the underlying disease and current risk factors and suggestions for lifestyle modifications. Based on the results of a recent synthesis of RCTs ($n = 8748$ people post-MI or revascularization), a psycho-educational approach should integrate several modes of delivery and preferably last for at least 3 months.[266] The effects of psycho-educational interventions on depression and anxiety symptoms when combined in meta-analysis are large based on accepted thresholds.[267]

For people with arrhythmias and/or ICD for primary or secondary prevention, there are physical symptoms, such as sleep disturbance, fatigue, and also psychological fears (fear of shocks, worry about the future, and fear of ICD dysfunction) affecting QoL. Psycho-education improved the physical component summary of QoL but had no effect on mental component summary scores.[268] In people with AF,

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reductions in serious adverse events [risk ratio (RR) 0.78; 95% CI 0.63–0.97], anxiety, depression, and health-related QoL (HRQoL) were observed with psycho-education, although the incidence of AF episodes was not affected.[269]

6.3.4. Social prescribing

Social prescribing is a transformative healthcare approach that connects people with non-medical resources to enhance their holistic well-being. The core idea behind social prescribing is to provide people with personalized interventions that extend beyond traditional medical prescriptions, encompassing a spectrum of community-based activities and resources.[270,271] The aim is to address diverse aspects of mental health, such as social isolation, loneliness, stress, and anxiety, by facilitating access to supportive community activities. Social prescribing leverages a variety of activities, ranging from arts workshops, music therapy, and group dance sessions to support networks, to enhance mental well-being and cultivate a sense of belonging and purpose.

Engagement in community activities, such as group dance, hiking, and cooking classes, combats feelings of isolation and fosters meaningful social interactions, thereby bolstering mental well-being.[272,273] These community connections act as protective factors against stress and isolation, potentially enhancing mental health support for people with CVD. This can lead to reductions in depressive symptoms, improvements in QoL, and better adherence to CV treatment plans.[270] A systematic review of 17 studies involving 13 social prescribing interventions with a total of 5036 participants found statistically significant improvements in mental health, general well-being, and QoL in 16 of the studies.[274] Despite these promising findings, more research focusing specifically on people with CVD is necessary to draw reliable conclusions.

Interventions involving social professionals were found to be more effective for reducing anxiety and depression, while those involving health professionals had a greater impact on improving blood pressure and encouraging physical activity.[275] Participating in arts, including visual art therapy and music therapy, has shown positive effects on mood and emotional regulation.[276] Music, in particular, can be a powerful tool in reducing stress and enhancing mood in people with CVD. Activities such as gardening, green exercise, and nature walks have been effective in reducing systolic and diastolic blood pressure and have demonstrated moderate to large effects on depression and anxiety scores.[275,277] These interventions also increase daily step counts, though the overall impact on physical activity time is still being evaluated.

Technology plays a pivotal role in facilitating social prescribing. Mobile apps and online platforms can recommend suitable social prescriptions based on personal profiles and mental health assessments, serving as valuable resources for people to explore options, engage in virtual support groups, and track their progress.[278] Real-time data collection through these platforms allows healthcare professionals to monitor engagement and outcomes more effectively.[279] Integrating social prescribing into standard care pathways, fostering community partnerships, and leveraging technology ensures efficient and personalized recommendations. This approach aligns with modern healthcare paradigms, emphasizing holistic well-being and personalized interventions, particularly for people with CVD dealing with mental health concerns, although more research is needed.[280] There is growing evidence supporting the use of social prescribing in the management of CVD. Healthcare professionals should be aware of local social prescribing interventions and availability in their environment and refer when appropriate.

6.3.5. Other psychological interventions

A Cochrane systematic review and meta-analysis of RCTs of psychological interventions for CHD including relaxation, cognitive techniques, emotional support and/or client-led discussion, and adjunct pharmacology, reported a reduction in CV mortality (from 7.3% to 5.5%) with psychological interventions compared with usual care controls.[281] No between-group differences were observed for the rates of total mortality, non-fatal MI, or revascularization procedures. Psychological interventions were found to achieve small to moderate improvements in depressive symptoms, anxiety, and stress compared with controls, although there remains some uncertainty in these estimates.[281]

Cognitive-behavioural therapy is a psychological intervention that focuses on changing patterns of unhelpful thinking and behaviour.[282] Two recent systematic reviews and meta-analyses assessing the efficacy of CBT-based interventions in RCTs in people with CAD showed that CBT-based interventions can reduce CV events, MI, and angina duration and intensity at the end of follow-up. Findings varied by trials, with no effect on other clinical outcomes,[283] but improving significantly psychological outcomes, such as depressive symptoms, anxiety, depression, stress, and increasing vital satisfaction at the end of follow-up.[284]

A recent study assessing the effect of CBT has shown efficacy in improving AF-specific QoL for people with symptomatic paroxysmal AF. AF-CBT led to large improvements, reducing healthcare-related consumption by 56%, although the AF burden remained unchanged.[285] A further RCT testing a CBT intervention in young people with CAD showed improvement in the total HADS score after 3 months, with differences maintained after 6 months. The intervention group also had greater adherence to ECR and more improvement in HRQoL at 6 months. A significant reduction in CVD-related admissions at 12 months was also observed.[286]

Recently, a multicentre study in which 250 people with AMI were randomized after PCI to either control or cognitive-behavioural stress management detected that the latter improves anxiety, depression, and QoL but does not affect MACE.[287] However, another trial of 362 people who had experienced a CVD event randomized to usual care or usual care plus CBT, found that CBT decreased the risk of recurrent events including MI.[288] Cognitive-based or external support coping mechanisms seem to attenuate the mental impact of PH, decreasing anxiety or depression rates.[289] This suggests a potential benefit for early identification and psychological intervention. In fact, psychosocial support has a Class I recommendation in the current ESC/European Respiratory Society (ERS) Guidelines for the diagnosis and treatment of pulmonary hypertension,[290] and is endorsed in the 2024 ESC Guidelines for the management of chronic coronary syndromes.[242]

Cognitive-behavioural therapy is safe and has shown to have beneficial effects in improving mental symptoms, in particular depression, and QoL in people with CVD and HF, and it could be a valid option due to the lack of potential side effects or drug interactions. However, a small qualitative study found that some people reported side effects, including discomfort with treatment and worsening of symptoms.[287,289,291]

Exposure therapy can be helpful for people with CVD, who due to their disease stop doing the things that they used to enjoy due to fear of another CV event, which may lead to depression. An example is a person who experiences an out-of-hospital cardiac arrest (OHCA) while cycling. Often this will cause anxiety and fear of taking up cycling again, as cycling is associated with OHCA. However, exposure therapy, where the therapist exposes the person gradually and in a safe way to situations and activities that they fear, is often helpful.[292]

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Similarly, behavioural activation uses behaviours to influence emotional state as engaging in activities that increase social connections and feelings of well-being can decrease depression. A pragmatic RCT in 416 people with HF and comorbid depression compared the effectiveness of antidepressant medication vs behavioural activation psychotherapy. Both groups experienced equal benefits with close to a 50% reduction in depressive symptoms at 3, 6, and 12 months.[293] People receiving behavioural activation psychotherapy had significantly better physical HRQoL and HF-specific HRQoL. Although there is limited evidence within CVD, some people have reported that philosophical counselling (Supplementary data online, *Table S8*) can be a complementary approach to other therapeutic strategies.

6.3.6. Interventions for people with post-traumatic stress disorder

Limited evidence on the prevention and management of CDI-PTSD is available. A comparison of eye movement desensitization and reprocessing (EMDR) with imaginal exposure in 42 people with PTSD induced by life-threatening CV events, including surgery, MI, and cardiac arrest, showed EMDR significantly reduced CDI-PTSD symptoms at 4 weeks and 6 months.[294] Fifty-one people with PTSD symptoms due to a CV event randomized to imaginal exposure or control group reported improved PTSD symptoms compared with the control group, although this difference was not statistically significant due to the small sample size. This initial study in the field of exposure psychotherapies provides promising evidence for the safety of using this technique in people with CVD.[295]

In a more recent RCT designed to determine if trauma-focused counselling within 48 h of hospital admission could prevent the development of PTSS, 190 people with ACS experiencing distress were assigned to either trauma-focused counselling (one session) or a general stress management active control group. Results showed fewer beneficial effects for the trauma-focused counselling group compared with the control group.[296]

6.3.7. Lifestyle interventions

Adopting a holistic approach that includes lifestyle changes can effectively improve mental health, CV well-being, risk factors, and CV outcomes.[297–302] Examples of lifestyle changes include regular physical activity, a balanced diet, stress management techniques (such as mindfulness and yoga), adequate sleep, and positive coping strategies.[303,304]

6.3.8. Physical activity and exercise in people with cardiovascular disease and mental health conditions

Physical activity encompasses a wide range of bodily movements that increase energy expenditure, including everyday tasks such as walking, household chores, and active commuting. Exercise is a more structured and purposeful form of physical activity designed to enhance or maintain physical fitness. The benefits of exercise in people with CVD extend beyond improving physical health; it also significantly enhances psychological well-being, including reassurance in those who are concerned for potential recurrences of their event or worsening of their disease. Exercise induces the release of endorphins and other neuroactive substances, contributing to mood improvement and stress reduction.[305] These effects are particularly beneficial for people with CVD, who often face psychological challenges in addition to their physical health issues.[306] In people with CAD and depression, exercise has been shown to be an effective component of treatment. A network meta-analysis (33 RCTs, $n = 7240$) demonstrated that exercise, when combined with antidepressants and psychotherapy, significantly reduced depressive symptoms at 8 weeks. The study suggested that while antidepressants remained effective at 26 weeks, the addition of exercise could enhance overall treatment efficacy.[307]

For people with HF, the Heart Failure-A Controlled Trial Investigating Outcomes of Exercise Training (HF-ACTION) demonstrated that exercise training led to a modest but significant decline in depression symptoms at both 3 and 12 months, as evidenced by improvements in the Beck Depression Inventory score in the exercise group. The study emphasized that while exercise is beneficial, the type and duration should be tailored to functional capacity, with considerations for independent or supervised exercise programmes.[308,309]

In summary, exercise is a critical component of managing CVD in adults, particularly for those with HF and CAD. Its benefits include improvements in both physical and mental health, which are crucial for enhancing the overall QoL in people with CVD.

6.3.9. Diet and nutrition approaches in cardiovascular disease and mental health conditions

Dietary interventions and nutritional strategies hold promise for improving both CVD[310] and mental health outcomes in individuals with CVD. However, the current evidence specifically addressing mental health improvements through dietary changes in this population is limited, highlighting the need for more robust and targeted research to establish clear recommendations.

Several dietary patterns have been explored for their potential mental health benefits in people with CVD. The Mediterranean diet, rich in fruits, vegetables, whole grains, and healthy fats, has been associated with lower rates of depression and cognitive decline in the general population, but data specific to people with CVD are still emerging.[311,312] Some studies suggest that the anti-inflammatory properties of this diet could be beneficial, yet conclusive evidence in CVD populations is lacking.[313,314]

Fasting interventions, including intermittent fasting and calorie restriction, have also been examined for potential to improve mental health. While some studies report encouraging results, such as improvements in mood and cognitive function, these findings are preliminary. The evidence is not yet strong enough to endorse one fasting method over another, particularly for individuals with psychiatric conditions.[314,315]

The Omega-3 Supplementation for Co-Morbid Depression and Heart Failure Treatment (OCEAN) trial reported that supplementation with eicosapentaenoic acid and docosahexaenoic acid in people with HF ($n = 108$) led to positive changes in cognitive depressive symptoms and social functioning. However, the small sample size and the use of soft endpoints suggest that these findings should be interpreted with caution, and larger, more definitive trials are needed.[316]

While dietary approaches and nutritional interventions are appealing for their potential dual benefits on CV and mental health in people with CVD, current evidence is insufficient to advise on diet interventions. More rigorous studies are needed to determine the most effective dietary strategies for improving mental health outcomes in this population.

6.3.10. Smoking cessation

Tobacco cessation offers significant CV health benefits, particularly for individuals with mental health conditions, including those with SMI. However, addressing tobacco use in this population is challenging due to the complex interplay between addiction and mental health issues. Sustained tobacco abstinence over 52 weeks can significantly reduce

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the 10 year CV risk in people with SMI.[317] Despite these CV benefits, individuals often face significant challenges post-cessation, such as notable weight gain, which can contribute to high rates of obesity, diabetes, and hypertension.[318] The addictive nature of tobacco use, especially in individuals with mental health conditions, necessitates treating tobacco use as an addiction and addressing it with comprehensive strategies.

Addressing tobacco cessation in individuals with mental health conditions requires a tailored approach. The Five A's model (Ask, Advise, Assess, Assist, Arrange) is a structured method commonly used to encourage and support tobacco cessation. However, it should be adapted to meet the unique needs of those with mental health conditions. For instance, healthcare professionals should be particularly attentive when assessing a person's readiness to quit, considering his or her mental health status, and providing additional support and resources that address both their tobacco use and mental health needs.

Cognitive therapies, when combined with medication, have been shown to improve tobacco abstinence rates in adults, including those with mental health conditions. A review of 21 RCTs found that cognitive therapies combined with medication or nicotine replacement therapy are more effective than medication alone, although the quality of evidence varied.[319] While tobacco cessation is crucial for improving CV and overall health in people with mental health conditions, it requires a nuanced and supportive approach that considers the complexities of addiction in this population.

6.3.11. Stress management techniques

Mindfulness,[320] meditation,[321] and progressive muscle relaxation[322–324] are stress management techniques that have shown promise in fostering cognitive resilience, emotional regulation, and relaxation. However, their specific effects on people with CVD need careful consideration and evidence-based discussion.[325–327]

Mindfulness involves focused attention on the present moment, fostering cognitive resilience against stressors and aiding emotional regulation.[320] A study of mindfulness on people with CVD showed improvements in psychological well-being and CV markers.[325] Mindfulness-based interventions for adults aged 19 to 40 years in developed countries, including mindfulness-based stress reduction programmes, mindfulness-based cognitive therapy programmes, and the Learning 2 BREATHE (Body, Reflections/thoughts, Emotions, Attention, Tenderness, Habits, Empowerment) programme, generally improve well-being and can be effectively implemented in a virtual format.[325]

Meditation focuses on controlled breathing or visualization, triggering the parasympathetic nervous system to induce relaxation and reduce stress hormones.[321] A meta-analysis indicated that distress management, when combined with ECR, offers limited additional effects, suggesting that meditation should be integrated cautiously with existing ECR programmes.[328] A further study showed that meditation can reduce stress and improve CV health outcomes in people with CVD.[326] Meditation and mindfulness, especially evidence-based forms like mindfulness-based stress reduction, can support people with CVD and their caregivers to reduce anxiety, depression, and pain. These practices have shown structural and functional brain changes, translate well across different populations, and offer a low-cost, beneficial method to complement treatment during this crisis.[326]

Progressive muscle relaxation involves sequentially tensing and releasing muscle groups to promote physical and mental relaxation, countering stress-induced physiological manifestations such as elevated heart rate, increased blood pressure, and muscle tension.[322–324] A study demonstrated that progressive muscle relaxation could reduce anxiety and improve heart rate variability in individuals with CVD.[327]

6.3.12. Sleep hygiene

Sleep quality is integral to both CV health and mental well-being, particularly in individuals with CVD. Poor sleep quality and insufficient sleep duration are linked to various adverse CV outcomes, including mortality,[329] atherosclerosis,[330] hypertension, impaired glucose metabolism, and increased inflammatory markers, and associated with an elevated risk of mental health conditions such as depression and anxiety, which can further complicate the management of CVD.[331–333] It is important for healthcare professionals to routinely inquire about sleep quality during clinical evaluations, given the significant impact of sleep on both CV and mental health. Interventions that improve sleep quality such as sleep hygiene measures and CBT for insomnia have been shown to improve mental health conditions.[331] Healthcare professionals should encourage people to adopt specific sleep hygiene practices, such as maintaining a consistent sleep schedule, avoiding stimulants like caffeine or nicotine close to bedtime, limiting screen exposure in the evening, and creating a restful sleep environment with minimal noise and light.[331] While wearables like smartwatches offer insights into sleep patterns, their diagnostic accuracy remains limited, and they should be complemented by validated clinical assessments and evidence-based interventions.

6.4. Tools and resources to support lifestyle change

6.4.1. Digital health tools

Among the many new mobile apps released every day for monitoring personal health data, only a minority have been scientifically validated on healthcare behavioural and clinical outcomes in the CV field. A systematic review encompassing 39 studies of wearable devices in multiple CVDs found potential benefits mainly in lifestyle aspects like physical activity and smoking cessation. However, the same review highlighted safety, reliability, and regulation concerns.[334] A systematic review and meta-analysis of mobile phone and mHealth interventions in people who had experienced a coronary event (20 studies, $n = 4535$) reported benefits in exercise capacity, physical activity, reductions in all-cause and CV readmissions, and improved physical and mental QoL.[335] A meta-analysis evaluating the efficacy of a digital health intervention in people with CVD showed that telemonitoring reduced depression in people with HF and CAD, and device-based psychological education and training had a significant positive effect in reducing depression in people with CAD or ICD. Although the use of information and communication technologies for health (eHealth) in daily practice is promising, there are still several barriers, including reimbursement challenges, digital literacy issues, and unequal access to digital technology (digital divide) in low-income countries or in remote areas as well as in the elderly.[336]

6.4.2. Motivational interviewing

Motivational interviewing (MotInt) is a person-centred counselling style for addressing the common problem of ambivalence about healthy lifestyle changes. It can be an effective counselling approach that bolsters motivation by resolving ambivalence. Motivational interviewing has shown efficacy in helping to make healthy behavioural changes and control CV risk factors with some evidence that shows an effect on the management of depression.[337] More information about MotInt can be found in the supplementary data online.

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6.4.3. Cardiac rehabilitation

Cardiac rehabilitation is a comprehensive multicomponent programme of secondary prevention aiming to reduce CVD risk and optimize health and well-being. A key component of most cardiac rehabilitation programmes is structured exercise (ECR) along with other components such as assessment, education, psychosocial support, information, behavioural interventions, and risk factor management.[338,339] Meta-analyses have shown that ECR is effective in improving mortality, morbidity, and HRQoL outcomes across multiple CV conditions,[340–344] but few meta-analyses provide evidence of improvement in measures of mental health.[343–345] These have found only weak evidence and small effects of ECR on depression and anxiety symptoms in people with CVD, even when psychological interventions were added.[328,344–346]

These results may be surprising given that psychosocial management is one of the core components of comprehensive ECR,[347] and exercise has been shown to have beneficial effects on the risk for and symptoms of depression and anxiety. Possible explanations include lack of systematic measurement of mental health outcomes, lack of recruitment of people with mental health conditions, and reluctance of people with mental health conditions to attend ECR or participate in studies. Screening for depression and anxiety in ECR is advocated,[348] but has been found to be inconsistently implemented with variation across conditions and services.[349] A position statement from the European Association of Preventive Cardiology (EAPC)[348] advises screening for mental health conditions and referral to a psychologist or psychiatrist when needed.

Exercise-based cardiac rehabilitation has the potential to benefit people with mild to moderate symptoms of depression, anxiety, and stress, but studies and evaluation are essential. One recent RCT trained ECR staff to deliver metacognitive therapy to people with CVD ($n = 332$) and demonstrated significant small to moderate improvement in depression and anxiety scores compared with ECR alone.[350] Suggestions for ensuring mental health benefit from ECR include:

- Screening for mental health conditions by ECR staff at the start and end of programme.
- Improving the implementation of screening through Guidelines combined with local/national initiatives to support screening.[351]
- Determining optimal interventions in ECR to improve symptoms of mental health conditions, including who should deliver these.
- Collaborating with mental health experts to ensure psychosocial support in ECR is robust and that referrals can be made when appropriate.
- Evaluating mental health symptoms as an outcome in ECR. The EAPC advocates a goal of improvement of depression and anxiety symptom scores by 10% on valid measures.[348]

6.5. Medical interventions

Medical interventions including pharmacotherapy may be needed for people with CVD with diagnosed mental health conditions and for people with severe symptoms of depression, anxiety, or PTSD. Careful assessment of the risks and benefits and open dialogue as recommended in *Section 6.3* will facilitate decision-making.

6.5.1. Efficacy and safety of pharmacological treatment for mental health conditions in people with cardiovascular disease

Studies evaluating the effectiveness of pharmacological treatment for mental health conditions in CV populations have shown inconsistent results. A systematic review and meta-analysis of 10 RCTs of antidepressant treatment following ACS found no general improvement in all-cause mortality and recurrent MI while the risk of repeat hospitalization was significantly reduced. However, in people with a concomitant diagnosis of depression, antidepressants decreased the odds of recurrent MI.[352] A Cochrane review examining trials on psychological treatments and antidepressant drugs in adults with CAD and comorbid depression concluded that pharmacological interventions may have a large effect on end-of-treatment depression symptoms, while effects on mortality or CV endpoints were deemed uncertain.[353]

Studies on the safety of antidepressant medication in HF have yielded conflicting results. One meta-analysis indicated that the use of antidepressants in people with HF is associated with an increased risk of all-cause death regardless of whether they have clinical depression or the type of antidepressants used.[354] In contrast, a recent meta-analysis reviewing studies of people with depression and known HF in both outpatient and hospital settings indicated that selective serotonin reuptake inhibitors (SSRIs) seem to be a safe treatment option.[355] This analysis, however, was limited by the variety of study designs and mixed results for different antidepressants.

Given the inconsistency of findings across studies on the effectiveness of pharmacological treatment for mental health conditions in people with CVD, there is a clear need for larger and robust RCTs. Concerns about drug safety, CV side effects, and interactions between psychiatric medications and CVD treatments complicate this management and need to be clarified in future research.

6.5.2. Use of specific medications in people with depression, anxiety, or post-traumatic stress disorders and cardiovascular disease

In the treatment of depression, anxiety, and PTSD, antidepressants are the first-line pharmacological treatment, while additional medications including anxiolytics, sedatives, and hypnotics, may be used in the short term. Other drugs, such as mood stabilizers and antipsychotics, may also be used, depending on the severity of symptoms. A brief description of the most common medications used for the treatment of mental health conditions is given in Supplementary data online, *Table S9*. *Figure 10* provides an algorithm for the pharmacological treatment of depression, anxiety, and PTSD in CVD.

6.5.3. Use of antidepressants

- The use of antidepressants in CVD populations requires careful selection of medications, dosage adjustments, and close monitoring due to potential side effects and clinically relevant drug interactions. In general, newer antidepressants are considered safe and associated with few serious long-term side effects in people with CVD.[356–358] However, CVD side effects may occur and are typically exerted through noradrenergic activation resulting from the use of serotonin and norepinephrine reuptake inhibitors (SNRIs), norepinephrine reuptake inhibitors, noradrenergic and specific serotonergic antidepressants, that can cause orthostatic hypotension or hypertension.[359]
- Weight gain (e.g. through mirtazapine use) may worsen CV risk.
- QTc prolongation can increase the risk of polymorphic ventricular arrhythmias, which has been associated with some tricyclic antidepressants (TCAs), SSRIs, and other antidepressants and bupropion, although the evidence is inconsistent.[360] A large population study did not find an increased risk of arrhythmias for citalopram.[361] A network meta-analysis demonstrated a low risk of ventricular

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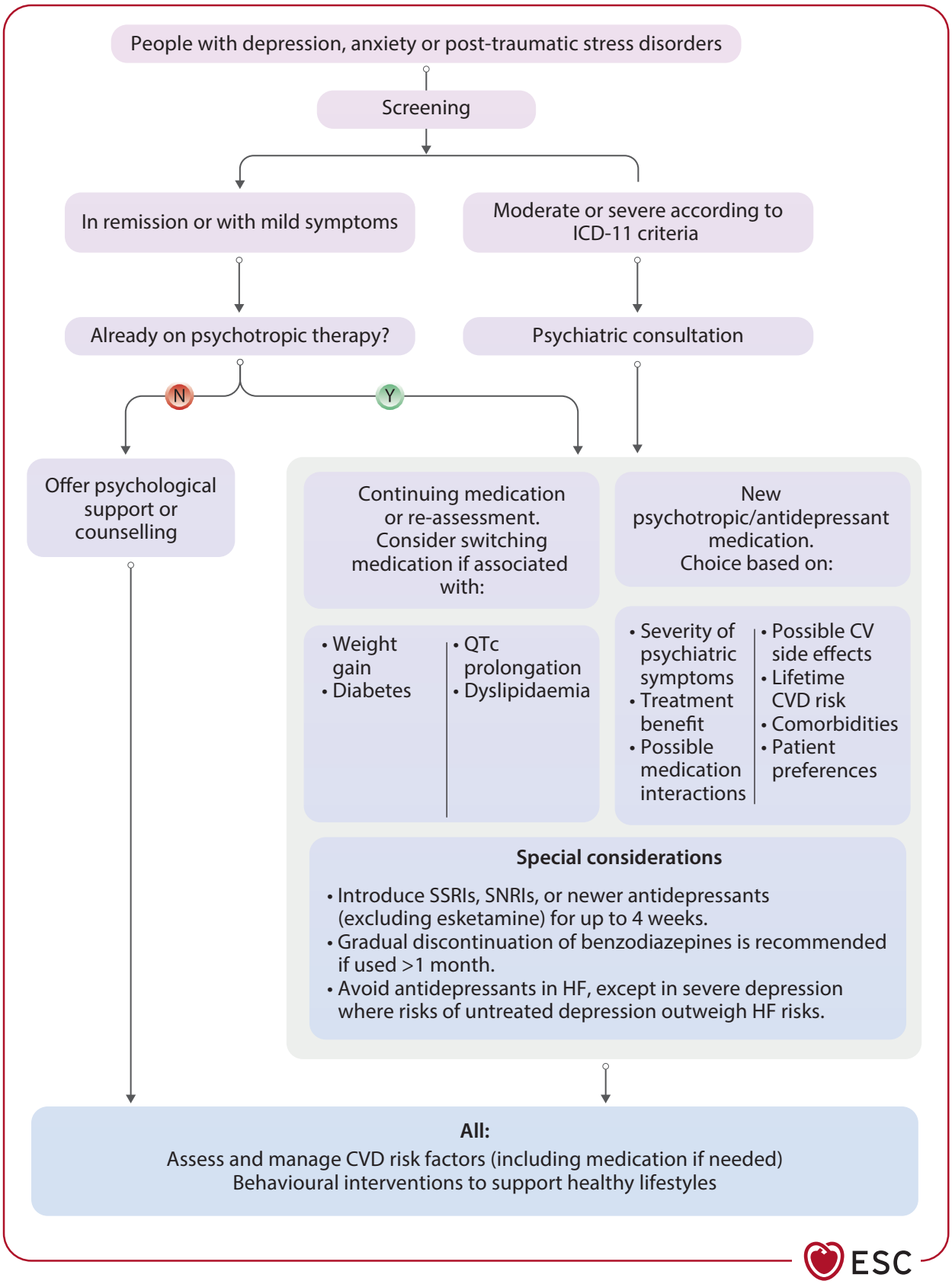
People with depression, anxiety or post-traumatic stress disorders
Screening
In remission or with mild symptoms
Moderate or severe according to ICD-11 criteria
Already on psychotropic therapy?
Psychiatric consultation
N
Y
Offer psychological support or counselling
Continuing medication or re-assessment. Consider switching medication if associated with:
• Weight gain
• Diabetes
• QTc prolongation
• Dyslipidaemia
New psychotropic/antidepressant medication. Choice based on:
• Severity of psychiatric symptoms
• Treatment benefit
• Possible medication interactions
• Possible CV side effects
• Lifetime CVD risk
• Comorbidities
• Patient preferences
Special considerations
• Introduce SSRIs, SNRIs, or newer antidepressants (excluding esketamine) for up to 4 weeks.
• Gradual discontinuation of benzodiazepines is recommended if used >1 month.
• Avoid antidepressants in HF, except in severe depression where risks of untreated depression outweigh HF risks.
All:
Assess and manage CVD risk factors (including medication if needed)
Behavioural interventions to support healthy lifestyles
ESC

Figure 10 Pharmacological management of cardiovascular disease and depression, anxiety, or post-traumatic stress disorders. CV, cardiovascular; CVD, cardiovascular disease; HF, heart failure; ICD, International Classification of Diseases; SNRI, serotonin and norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

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arrhythmia and SCD among people using antidepressants like SNRIs, SSRIs, and especially TCAs.[362] Some antidepressants (mirtazapine, venlafaxine, trazodone) were not found to prolong the QTc interval in healthy volunteers.[363–365]
- Reduction of heart rate variability has been associated with TCA use.[366,367]
- Temporary increase in blood pressure immediately after administration has been described with esketamine, which is indicated for treatment-resistant depression, however, it is not associated with long-term development of hypertension.[368]

Importantly, several pharmacokinetic and pharmacodynamic interactions between antidepressants and CV drugs may affect the efficacy and safety of treatment. Therefore, therapeutic drug monitoring, defined as the measurement and interpretation of drug concentrations in blood to optimize pharmacotherapy, is proposed in special clinical scenarios. It is particularly useful in cases of non-response at therapeutic doses, uncertain drug adherence, suboptimal tolerability, or pharmacokinetic drug–drug interactions. In people with mental health disorders, therapeutic drug monitoring has additional applications ranging from strongly recommended to potentially useful including use in children and adolescents, pregnant women, elderly people, individuals with intellectual disabilities, people with substance abuse disorders, forensic psychiatric conditions, or people with known or suspected pharmacokinetic abnormalities.[369]

Many antidepressants and CV drugs are metabolized by cytochrome P450 (CYP) enzymes leading to potential interactions, which are dose dependent and can be exaggerated by smoking (Supplementary data online, *Table S10*). Smoking is a potent inducer of CYP1A2 enzymes with maximal increase by 10 or more cigarettes per day and decrease of CYP1A2 activity within 3 days after smoking cessation.[370,371] Potential risks for interactions between antidepressants and CV drugs include beta-blockers and calcium channel blockers. For example, SSRIs inhibit the enzyme activity phase of the CYP pathway by blocking the active site of certain CYP isoenzymes, thereby reducing the metabolism of other drugs. This may lead, for example, to increased plasma levels of metoprolol with a risk of bradycardia or hypotension. Furthermore, amiodarone inhibits CYP2C9, CYP2D6, and CYP3A4, leading to potential interactions with both SSRIs and TCAs, requiring careful monitoring for side effects.[369]

Notably, SSRIs and SNRIs can increase bleeding risk.[372] However, there is little evidence that SSRIs increase the risk of clinically relevant bleedings or mortality.[373] Further, SSRI interactions via the CYP isoenzyme system can potentially increase the effects of warfarin and thus, the risk of major bleeding requiring close monitoring and management of risk factors for bleeding in people treated with both SSRI and vitamin K antagonists like warfarin.[374] Although studies suggest that direct oral anticoagulants have lower potential for pharmacokinetic interactions with SSRIs, caution is also required with concomitant use of SSRI and direct oral anticoagulants, which showed a similarly increased risk of major bleeding as vitamin K antagonists.[375,376] Potential interactions between antidepressants and drugs for SMI are summarized in Supplementary data online, *Table S9*.

6.5.4. Use of anxiolytics, sedatives, and hypnotics

Anxiolytics, sedatives, and hypnotics may be used to manage symptoms like anxiety and insomnia, which are common in the CVD population. However, potential benefits need to be balanced against risks, especially with long-term or high-dose use. If used, clinical evaluation should include assessment for suitability to switch to a safer alternative like SSRIs for anxiety, or CBT for insomnia. Further, these drugs are overused and overprescribed worldwide in the general population and especially among the elderly and people with mental health conditions.[377] Benzodiazepine prescription, especially long-term or daily use, has been linked to an increased risk of all-cause mortality.[378,379] These findings may be partly explained by residual confounding.[380] Some studies also suggested that benzodiazepines may elevate the risk of CV events and mortality, particularly in older adults.[381]

6.5.5. Pharmacological treatment for mental health conditions in specific cardiovascular diseases

6.5.5.1. Ischaemic heart disease

Pharmacological treatment for IHD in people with mental health conditions aims to reduce the symptoms of mental health conditions, improve CV outcomes, and reduce modifiable CV risk factors. In general, it is preferable to avoid benzodiazepines routinely for managing AMI,[382] and to be cautious about adding medications given the potential for interactions and possible side effects. In people who smoke, bupropion or varenicline can be used as they are effective and safe in reducing smoking in the short term.[383,384] If a person with depression is being treated with mirtazapine, switching to other antidepressant drugs with less propensity to induce weight gain may be considered, in consultation with psychiatrists.[356]

6.5.5.2. Ventricular arrhythmias

In people with ventricular arrhythmias, it is necessary to evaluate the link between arrhythmias and the use of reported antidepressants. In the context of clinical suspicion, it is preferable to switch to drugs with less propensity to cause ventricular arrhythmias. Several antidepressants have shown a potential to change ventricular repolarization:

(i) Citalopram/escitalopram possibly increase the risk of QTc prolongation in dosages over 20 mg compared with placebo.
(ii) TCAs are associated with increased risk of QTc prolongation compared with newer antidepressants.

For more information on QTc prolongation associated with psychotropic drugs see *Section 7.6.1*.

6.5.5.3. Heart failure

In people with HF, the efficacy of antidepressant and/or antipsychotic drugs is not well established.[385] Therefore, careful assessment of risks and benefits should be performed by a multidisciplinary Psycho-Cardio team before initiation. Indeed, despite mental health conditions increasing the risk for adverse outcomes and mortality in people with HF, the indiscriminate use of antidepressants may increase the risk of CV side effects and drug interactions, especially among the elderly or frail. This is well summarized in a position paper endorsed by the EAPC.[386] In addition, the use of antidepressants has been associated with an increased risk for all-cause and CV mortality, irrespective of the presence of clinical depression.[354,387]

If antidepressants are needed:

- SSRIs are considered the safer class of antidepressants to use in HF as they are associated with fewer adverse CV side effects (less likely to cause orthostatic hypotension or tachycardia, little effect on intraventricular conduction).[388] However, SSRIs can cause QTc prolongation, especially citalopram and escitalopram (but also sertraline and fluoxetine), can increase the bleeding risk in elderly people receiving antiplatelet or anticoagulant medications through their inhibition of platelet aggregation/activation, and enhance gastric acid secretion.[372,389,390]

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- Due to their minimal inhibition of CYP enzymes, sertraline, citalopram, and escitalopram have a lower risk of drug interactions compared with fluvoxamine, fluoxetine, and paroxetine.
- Monoamine oxidase inhibitors and TCAs should be avoided for the treatment of depression in HF as they may cause orthostatic hypotension, worsening HF, and ventricular arrhythmias.[391]
- Venlafaxine and duloxetine should be used with caution in people with HF due to the small and contradictory evidence.[392]

The use of antidepressants in people with HF should be restricted to those with severe depression, where the risk of untreated depression outweighs the risk of taking antidepressants. The use of specific drugs for the treatment of HF can also be associated with the development of depression/anxiety: diuretics and nitrate esters are associated with a higher risk of depression in people with HF,[393] while no increased risk of depression has been reported for beta-blockers (especially for the hydrophilic form since they do not significantly cross the blood/brain barrier), statins, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, aspirin, aldosterone antagonists, and sodium–glucose co-transporter-2 inhibitors.[393,394]

6.5.5.4. Procedures (coronary artery bypass grafting, percutaneous coronary intervention)

In general, the use of benzodiazepines is not indicated for PCI or coronary artery bypass grafting, but this consideration is based upon low-quality evidence.[395,396] No specific recommendations are available for the use of psychotropic drugs.[395]

6.6. Organization of care

Healthcare is frequently fragmented by specialties, hindering efforts to provide holistic care that addresses physical and mental health conditions. New care models have sought to integrate physical healthcare into mental healthcare settings, and mental healthcare into settings focused on physical conditions.[397] Novel integrated programmes using remote delivery of mental health interventions and promoting psychological well-being have garnered growing interest in the literature.[398]

Several RCTs have explored the effectiveness of collaborative care models in managing various health conditions. Co-ordinated or collaborative care of people with CVD and other conditions has been shown to improve CV risk factors, cardiometabolic disease control, general function, and symptoms of depression.[399–402] A systematic review and meta-analysis of collaborative care in primary or community healthcare settings (79 trials) reported significantly greater improvements in depression and anxiety in the short and long term, along with increased medication use, mental health components of QoL measure (SF-12, SF-36), and satisfaction.[403] However, an RCT of a collaborative care programme for people with HF and depression did not show significant improvements in clinical outcomes compared with enhanced usual care.[404] An integrated adult congenital heart disease (ACHD) psychology service has been shown to reduce psychological distress, however, few people received full psychological assessment.[405] A recent position paper addresses the main mental health concerns in congenital heart disease and advocates the generation of models for the integration of mental health professionals in paediatric and ACHD teams.[406]

Although often delivered in primary care, collaborative care models have also been evaluated in rehabilitation facilities,[407,408] and acute care hospitals.[409] Collaborative care has been tested in mental health clinics and was found to improve physical health compared with usual care with no differences in overall QoL. Half of the effects on functioning were mediated through the effects of collaborative care on depression severity in people with bipolar depression.[410,411]

Collaborative care is usually delivered by nurses supported by a multidisciplinary team. Further study of novel applications of collaborative care and related interventions is warranted due to the potential of these programmes to improve management of CVD and mental health conditions and enable CV practices to deliver holistic care.[398] In particular, new models of integrated care with multidisciplinary teams (Psycho-Cardio team) and experts in improving mental health are needed in clinical CV care. The composition and function of these teams should be dynamic and flexible, adapted to the needs of people with CVD, their caregivers, clinical scenarios, and available resources.

6.7. Section summary points and management consensus statements from *Section 6*

SECTION SUMMARY POINTS

(i) Ideally, assessment of mental health status should be performed routinely within CVD clinical practice and implemented when the context of local capacity and capability allows.

(ii) Depression and anxiety can easily be overlooked in the routine care of people with CVD and/or considered 'normal' reactions to individual clinical/prognostic burden of disease.

(iii) Clinical history can be used to identify mental health symptoms. If there is clinical suspicion, formal screening with validated tools is advised.

(iv) Psycho-Cardio teams are needed to structure pathways for:
- Screening.
- Referral.
- Treatment of people with CVD and suspected or established mental health conditions.

(v) Medical interventions including pharmacotherapy may be needed for people with CVD who are diagnosed with mental health conditions, especially for severe symptoms of depression, anxiety, or PTSD.

(vi) In some people with CVD, combination therapy of psychological interventions plus medication may be useful.

Continued

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MANAGEMENT CONSENSUS STATEMENTS

(i) Screening of mental health with validated screening tools is advised after a new diagnosis or CV event, at least once during follow-up and anytime based on clinical judgement of need.

(ii) Initial simple screening with a two-item measure (i.e. Whooley questions, PHQ-2, GAD-2) can be incorporated into routine practice.

(iii) A low threshold for mental health screening in people with CVD is advised, considering the high prevalence of mental health conditions in people with CVD and its impact on outcomes.

(iv) Following an abnormal result in the initial screening, a longer validated screening instrument should be used to determine if condition severity is low, moderate, or high.

(v) Psycho-Cardio teams must define who is responsible for the assessment of mental health conditions and how and when it will be done, tailoring it to the specific context and resources.

(vi) Each Psycho-Cardio team may choose a particular screening tool after careful assessment of its validity, reliability, and applicability to their population, but standardized screening tools are preferred for mental health assessment.

(vii) People scoring high on a screening questionnaire need referral for diagnostic assessment and appropriate treatment by a mental health professional.

(viii) Applying a stepped care approach to manage mental health conditions in people with CVD is reasonable based on preferences, severity of symptoms and condition, and resources available.

(ix) Developing and evaluating tailored intervention programmes aimed at alleviating distress of people coping with CVD and caregivers may be useful.

(x) Lifestyle measures and psycho-education are useful for all people with CVD while psychological therapies may be helpful for people experiencing depression and/or anxiety.

(xi) Cardiac rehabilitation is an opportunity to screen people for depression and anxiety and can contribute to improve mental health after CV events or be an opportunity to identify and manage mental health conditions.

(xii) Avoiding benzodiazepines as first-line therapy in the management of anxiety and depression is advised.

(xiii) Anxiolytics, sedatives, and hypnotics are overused and overprescribed in the general population, especially among the elderly and people with mental health conditions, so careful selection of indications is advisable.

(xiv) Antidepressant use is advised for those with moderate to severe anxiety disorders and depression under the guidance of qualified mental health professionals.

(xv) The use of antidepressants in HF is only advisable in severe depression symptoms where the risk of untreated depression outweighs the risk of taking antidepressants.

(xvi) In people with ventricular arrhythmias, antidepressants associated with an increased propensity to prolong QTc (such as TCAs and possibly citalopram/escitalopram in dosages over 20 mg), may be switched to newer antidepressants with better safety profiles.

(xvii) Given the frequent interactions between antidepressants and CV drugs affecting their efficacy and safety, therapeutic drug monitoring is advisable to optimize pharmacotherapy and minimize potential side effects and clinically relevant drug interactions.

7. Severe mental illness and cardiovascular disease

7.1. Cardiovascular risk in people with severe mental illness

Severe mental illnesses are diseases defined by a significantly impaired level of psychosocial functioning and usually comprise disorders such as schizophrenia, bipolar disorder, and severe recurrent major depressive disorder[6] (*Figure 11*). Definitions and characteristics of SMI according to ICD (International Classification of Diseases)-11 criteria,[7] can be found in Supplementary data online, *Table S11*.

Individuals with schizophrenia and bipolar disorder have been found to live approximately 14.5 and 8–12 years less than their counterparts without SMI, respectively.[412,413] All-cause mortality in people with SMI is more than 2.5 times higher compared with the general population,[414] and the standardized mortality gap may be increasing over time.[415] Cardiovascular disease plays a major role in cause-specific mortality among people with SMI,[26] and SMI increases the incidence and prevalence of CVD. People with schizophrenia are at two- to three-fold higher risk of having CVD, particularly younger individuals.[12] In a large-scale meta-analysis (3 211 768 people with SMI; 113 383 368 controls), the pooled prevalence of CVD was 9.9% and the cumulative incidence of CVD was 3.6% in people with SMI (median follow-up 8.4 years), a significantly higher adjusted risk of CVD incidence compared with controls in longitudinal studies.[12] People with schizophrenia have significantly higher rates of SCD, exceeding population rates by 11-fold.[416] There is some evidence to suggest young adults with SMI may be at particular risk of increased CV events.[417,418]

7.2. Prognosis in severe mental illness and cardiovascular disease

The co-occurrence of SMI and CVD increases all-cause mortality risk and worsens CV prognosis. Observational studies suggest that, among people with SMI, the risk for CHD and CV mortality is up to 2.5 times higher in people with schizophrenia and bipolar disorder compared with controls, with larger effects in younger people.[419] According to Danish national registry data, while trends in MI mortality rates declined over 1 and 5 years of follow-up, people with schizophrenia did not experience the same decline in mortality rate following MI in long-term follow-up.[420] People with SMI present clinically with HF 7 years earlier than the general population, and men with SMI and HF have excess mortality compared with men with HF without SMI. ICD implantation, cardiac resynchronization therapy, VAD implantation, and HTx are used at a similar rate in people with HF with reduced ejection fraction and SMI as those without SMI, but people with SMI experienced poorer prognosis following cardiac resynchronization therapy, VAD, and HTx.[421]

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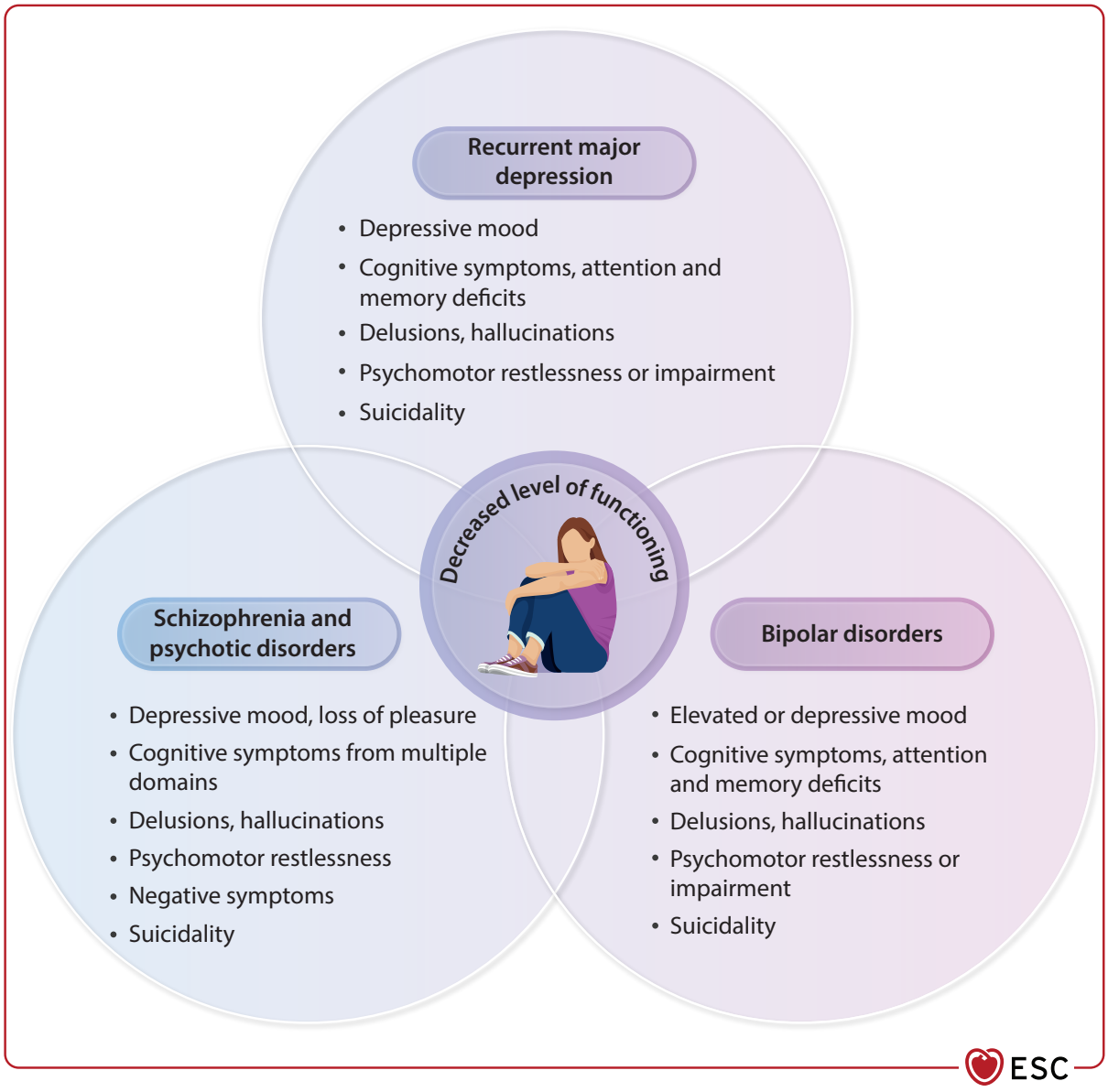

Figure 11 Severe mental illnesses.

7.3. Increased cardiovascular disease risk in people with severe mental illness

The aetiology of CVD in people with SMI is multifactorial, involving genetic/biological, disease-specific and treatment-specific effects, lifestyle factors, and treatment disparities, which are mutually intertwined.[422,423] A summary of these factors is given in *Figure 12*, and described in the text below.

7.3.1. Lifestyle and biological risk factors

Risk factors including hypertension, diabetes mellitus, dyslipidaemia, obesity, and smoking, contribute to a significantly higher CV risk in people with SMI.[424,425] Genetic/biological, disease-specific factors include common genetic vulnerability for schizophrenia and diabetes, the effects of psychopathology such as negative and depressive symptoms leading to sedentary lifestyle.[424] Schizophrenia is associated with more than a three-fold risk of obesity compared with the general population,[426] and metabolic syndrome and diabetes were also found to be more prevalent in people with schizophrenia and bipolar disorder.[426–429] Hypertension was found to be more prevalent in people with bipolar disorders, but not schizophrenia.[430] Finally, people with schizophrenia had five times higher odds of smoking than the general population,[431] up to 65% of people with schizophrenia are smokers,[432,433] and they have higher rates of alcohol addiction.[434] People with SMI have not shown the same reduction of modifiable risk factors and resulting decrease in CVD mortality rates as the general population.[419]

7.3.2. Medication-induced cardiovascular risk factors

Disease-specific and medication-induced factors include side effects to medications, obesity, diabetes, hypertriglyceridaemia, and hypercholesterolaemia.[427,435–438] The effect of medication is not straightforward, as metabolic-induced side effects may not be independent predictors for

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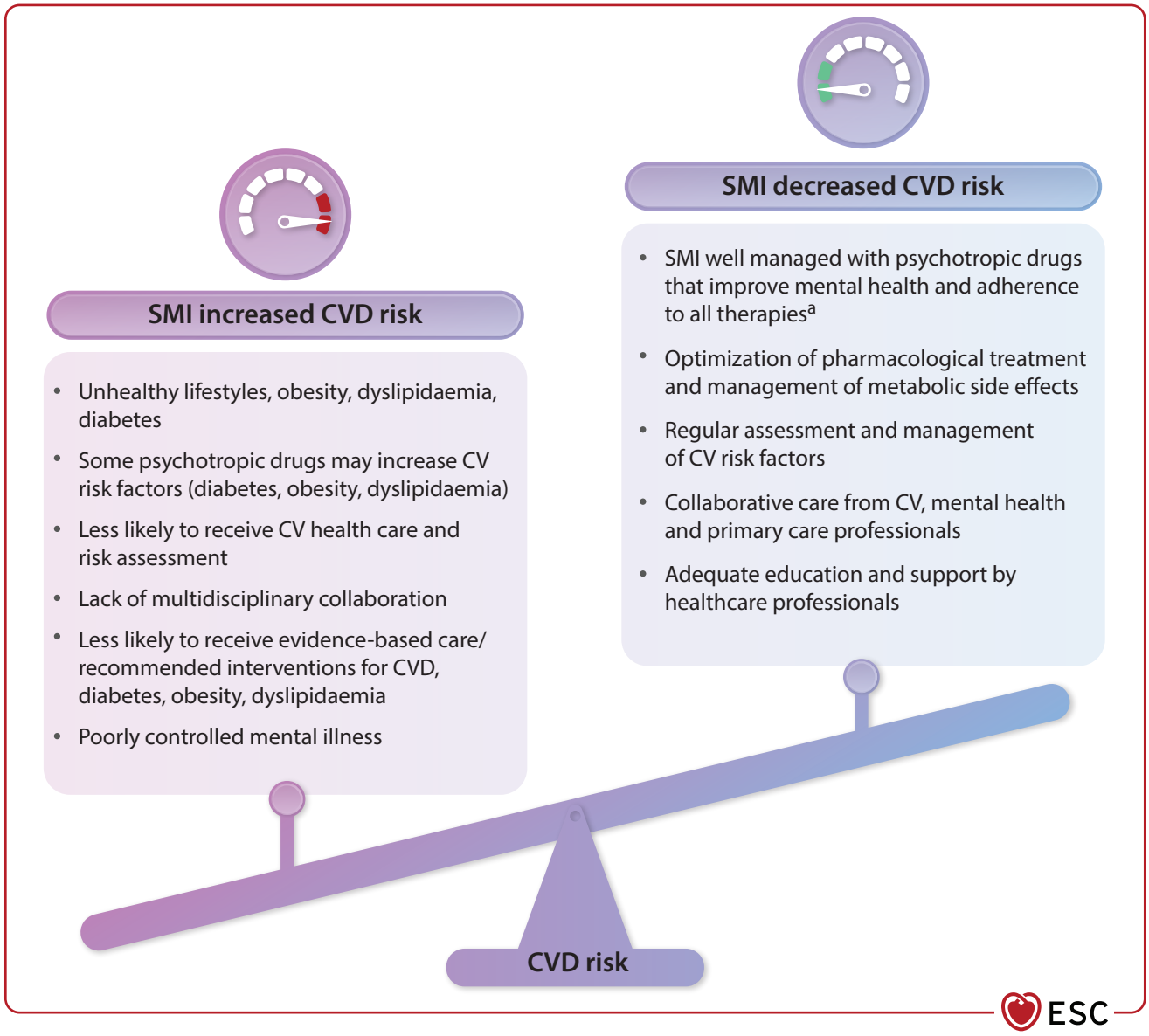
SMI increased CVD risk
Unhealthy lifestyles, obesity, dyslipidaemia, diabetes
Some psychotropic drugs may increase CV risk factors (diabetes, obesity, dyslipidaemia)
Less likely to receive CV health care and risk assessment
Lack of multidisciplinary collaboration
Less likely to receive evidence-based care/ recommended interventions for CVD, diabetes, obesity, dyslipidaemia
Poorly controlled mental illness
SMI decreased CVD risk
SMI well managed with psychotropic drugs that improve mental health and adherence to all therapies[a]
Optimization of pharmacological treatment and management of metabolic side effects
Regular assessment and management of CV risk factors
Collaborative care from CV, mental health and primary care professionals
Adequate education and support by healthcare professionals
CVD risk
ESC

Figure 12 Multifactorial aetiology of cardiovascular disease risk in people with severe mental illness. CV, cardiovascular; CVD, cardiovascular disease; SMI, severe mental illness. [a]Choose psychotropic drugs less likely to cause obesity and metabolic risk.

CVD in persons with SMI.[438,439] A summary of data on CV risk associated with antipsychotic use is highlighted below:

- Current reports do not show that antipsychotics are associated with increased risk of MI or stroke in people with schizophrenia and bipolar disorder compared with placebo,[440] despite previous meta-analyses.[12,441]
- The use of long-acting antipsychotic medication and second-generation antipsychotics were found protective against all-cause mortality compared with no antipsychotic use. The largest effects were seen for second-generation long-acting injectable antipsychotics, clozapine, any long-acting injectable antipsychotics, and any second-generation antipsychotics.[26] In a Finnish nationwide database study (median follow-up 14.1 years), CV mortality was significantly lower among patients with schizophrenia on any antipsychotic treatment compared with non-use. Several antipsychotics were associated with a significantly reduced CV death risk compared with non-use (long-acting injectable olanzapine and oral flupentixol) and the use of clozapine reduced all-cause mortality by 61% and CV death risk by 45% compared with non-use of antipsychotics.[442] Findings were possibly explained by improved adherence to antipsychotics of people with SMI, as this has been associated with decreased discontinuation risk of antidiabetics, statins, antihypertensives, and beta-blockers in people with schizophrenia.[443] The use of medication appears not to influence the cardiorespiratory fitness level of people with SMI receiving treatment.[444]

Antipsychotics vary in their propensity to induce modifiable CVD risk factors. Most second-generation antipsychotics with wide receptor activity profiles (serotonin 5-HT_{2A}, histamine H1, muscarinic M3), such as olanzapine, clozapine, and quetiapine, are associated with increased risk of weight gain and consequent metabolic syndrome, weight gain-related diabetes, and hypertriglyceridaemia.[437] According to a meta-analysis of RCTs, olanzapine, clozapine, zotepine, sertindole,

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Table 6 Summary of the negative effect of different antipsychotics on cardiovascular risk factors

Drug	Weight gain	Hyperglycaemia	LDL cholesterol	HDL cholesterol	Total cholesterol	Triglycerides
Haloperidol	0	++	ND	ND	++	++
Ziprasidone	0	+	0	0	+	+
Aripiprazole	+	++	+	+	++	+
Lurasidone	+	0	+	+	+	+
Cariprazine	+	++	0	+	0	+
Fluphenazine	+	ND	ND	ND	ND	ND
Amisulpride	+	0	ND	+++	++	++
Brexpiprazole	+	+	++	0	++	0
Flupentixol	+	ND	ND	ND	ND	ND
Asenapine	++	0	ND	ND	ND	ND
Risperidone	++	+	++	++	++	+
Paliperidone	++	+	++	++	++	+
Quetiapine	++	+	+++	++	+++	++
Iloperidone	++	++	ND	ND	+	++
Sertindole	+++	+	ND	ND	++	+
Zotepine	+++	+++	ND	ND	ND	+++
Clozapine	+++	+++	ND	ND	+++	+++
Olanzapine	+++	++	+++	+++	+++	+++

HDL, high-density lipoprotein; LDL, low-density lipoprotein; +, strength of effect; ND, no data.

iloperidone, and quetiapine were found to be associated with worse metabolic profiles (weight gain, glucose increase, hypertriglyceridaemia, hypercholesterolaemia, and decrease of high-density lipoprotein cholesterol) in short-term use.[435] Zotepine, olanzapine, sertindole, cariprazine, iloperidone, quetiapine, clozapine, and risperidone have been associated with the greatest weight gain (up to 3 kg), but nearly half of antipsychotics caused significantly more weight gain than placebo.[445,446] A summary of effects of antipsychotics on CVD modifiable risk factors is presented in *Table 6*.

7.3.3. Assessing cardiovascular disease risk

Widely used tools for CV risk assessment in the general population usually underestimate the risk of CVD in the population with SMI.[447] Significant differences in risk prediction screening tools such as metabolic syndrome concept, Systematic Coronary Risk Evaluation (SCORE) model and two PRedIction and Management of cardiovascular Risk in peOple with SEvere mental illnesses (PRIMROSE) models, carry the risk of significant disparities in treatment initiation in people with SMI.[447] Moreover, these models generally underestimate CV risk in adolescents with SMI.[447,448] Finally, there is no consensus of which healthcare professionals should screen and monitor for CVD in SMI. While screening is usually in the domain of primary care, persons with SMI have overall low use of health services, therefore, mental health professionals may need to take the lead for screening,[21] diagnostics,[22,23] and treatment.[21,24–26]

Several practice Guidelines for the screening and monitoring of CV risk in people with schizophrenia are proposed but have been scarcely implemented. Position statements by the European Psychiatric Association, supported by the European Association for the Study of Diabetes (EASD), and the ESC have made recommendations for screening.[449] We highlight the following as particularly important for people with SMI and CVD:

- Routine screening for CVD risk factors should be performed by psychiatrists and general practitioners at all stages of the disorder, regardless of age, with initial risk assessment carried out during the first visit and before the prescription of antipsychotics. Baseline risk assessment includes:
  - Personal and family history of CVD or diabetes or related disease.
  - Lifestyle patterns: smoking and alcohol consumption, healthy diet, physical activity.
  - Weight, height, waist circumference, calculation of body mass index.
  - Fasting blood glucose and lipids (total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides).
  - Blood pressure, heart rate.
- All individuals with SMI taking antipsychotics should be actively monitored for modifiable risk factors at baseline, after 12 weeks, and at least annually thereafter.
- People who have CV risk factors should be monitored at the start of a new treatment and re-assessed 6 and 12 weeks after initiation of a new antipsychotic drug, and periodically, depending on the presence of risk factors.[449] In people with diabetes, monitoring should include glycated haemoglobin every 12 weeks.
- After initiation of antipsychotics known to induce CV side effects [e.g. prolongation of QTc interval or tachycardia (see *Section 7.6.1*)], electrocardiogram (ECG) is advised at baseline, after 1 week, and after 6 and 12 weeks, and annually thereafter.

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7.4. Gaps and disparities in the management of cardiovascular disease in people with severe mental illness

The presence of SMI in itself does not explain the lifespan inequalities observed.[450] Multiple factors have been identified including systemic barriers to prevention,[310] screening,[21] diagnosis,[22,23] and treatment.[21,24–26] Collectively, these lead to large healthcare disparities for people with SMI. Key studies confirm these inequalities persist in CVD.[451–454] To overcome these barriers healthcare professionals need to be aware of, and address, system-level problems including stigma, stereotypes, prejudice, and diagnostic overshadowing (defined as the misattribution of physical symptoms to pre-existing psychological illnesses).[455]

7.4.1. Autonomy, communication, and informed consent

Communication between the CV team and people with SMI and CVD should follow similar principles as for people with CVD without SMI outlined in *Section 6.3*. For people with SMI, this may require a move away from the established 'best interest' approach (healthcare professionals know what is best), to a 'will and preference' approach which prioritizes goals and values.[456] This shift is particularly critical for people with SMI and CVD, who may experience heightened stigma or bias that can lead to paternalistic treatment. Respecting their will and preference not only affirms their human right to self-determination and dignity, but also allows them greater control over their care, promoting a sense of ownership in managing their health. The Psycho-Cardio team should develop a more proactive and person-centred approach in caring for persons with SMI including:

- Educating the people about their illness, warning signs, treatment, and management plan.
- Including people with SMI and family/caregivers in the management plan using SDM.
- Engaging people with SMI to participate in their care actively by including them in all forms of treatment (lifestyle modification programmes, smoking cessation).
- Encouraging people with SMI to check up regularly for CVD risks and CV symptoms.
- Monitoring adherence to medication.
- Reassuring and signposting to practical information or resources.
- Asking if there is someone the person with SMI would like you to contact.

People with SMI are presumed to have capacity to consent to treatment unless there is reason to believe this is not the case. In those rare situations, a decision-making capacity assessment may be required, and this should be undertaken by the professionals involved in delivering the physical health intervention being proposed. Depending on jurisdiction, people with SMI may have appointed a decision-maker themselves or may have an advanced healthcare directive, so it is important to be aware of these issues and determine a person's capacity to consent to treatment before proceeding.

If the person with SMI already has a legal guardian, they have the legal authority to sign medical informed consent, but different acts may be applied in different countries. People with SMI may have reduced ability to participate in the treatment processes due to the nature of SMI leading to unintentional non-adherence. In severe active psychosis, the individual may not be able to communicate CV symptoms or may not be able to tolerate invasive investigations and/or therapies because of psychiatric symptoms.

Many people with SMI may become suitable for an invasive strategy and be clinically assessed for CV interventions. This may require an advocating and assertive approach by the management team, and close collaboration with liaising mental health professionals and general practitioners. The management of CAD in people with SMI should be discussed by the Psycho-Cardio team (*Figure 3*), with input from a psychiatrist. Many deficiencies in the management of CAD in people with SMI occur for obvious and at times insurmountable reasons. Consensus and collaboration among people with SMI, families, general practitioners/family physicians, CV specialists, and mental health professionals is essential for good practice. General practitioners play a particularly relevant role in reviewing and optimizing the physical and mental health of people with SMI and CVD, being responsible for the integral process of care and co-ordinating care by the different specialists involved.

In the care of SMI, flexible assertive community treatment models usually ensure better availability of health services for persons with SMI and prominent psychiatric symptoms, but there is a lack of studies analysing the effects of these models in people with CVD.[457,458] Interactive telemedicine (therapy delivered via video conferencing) was found comparable to in-person delivery in effectiveness, acceptability, and cost in people with various mental health and substance abuse issues.[459]

7.5. Management of cardiovascular disease in people with severe mental illness

7.5.1. Management of modifiable risk factors

Management of modifiable risk factors in people with SMI follow the same principles as in people without SMI, such as education, behavioural counselling, lifestyle interventions, and peer and family support interventions. Increased efficacy of interventions directed to improve CV risk in people with SMI is associated with:

- High intensity and high co-ordination.
- Inclusion of both behavioural and pharmacological management, following a multimorbidity approach.

Few studies, however, have evaluated interventions addressing one or more CVD risk factors in people with SMI.

7.5.2. Diet, physical activity, and body weight control

The diet of people with schizophrenia is often unhealthy, characterized as being poor in fibre and fruit, and rich in saturated fats with a high caloric intake.[460] People with SMI are generally less physically active than the general population, performing significantly lower volumes of moderate to vigorous activity per day according to a meta-analysis of 69 studies.[424] Currently available studies in people with SMI indicate a beneficial effect of exercise and diet on CV risk, with interventions increasing weekly activity compared with no intervention.[461] Significant improvements in fitness, psychiatric symptoms, and overall functioning were found in participants who attended 50% of physical activity sessions.[462] The European Psychiatric Association (EPA) suggests that

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physical activity should be regularly offered to people with SMI as a low risk and accessible way of improving health.[463]

In general, weight loss should be advised to people with SMI who have a body mass index ≥25 kg/m^2 or a waist circumference ≥88 cm in women or ≥102 cm in men.[449] The effectiveness of behavioural or integrative interventions to improve CV risk in people with SMI has had mixed results.[422] Two of four studies reported a decrease in CV risk in the integrated care intervention group compared with control groups, however, two studies reported no difference.[464–467]

Glucose and lipid-related laboratory results were mainly reported as secondary outcome assessments in studies of weight management interventions. Metformin is the currently accepted first-line treatment of antipsychotic-associated weight gain, although not all people benefit.[468] In 2020, the ESC in collaboration with the EASD updated their treatment algorithms to recommend the use of glucagon-like peptide-1 receptor agonists and sodium–glucose co-transporter-2 inhibitors as alternate therapy options to metformin based on CV and renal comorbidities independent of glycaemic control. However, there are still no data to support their use for antipsychotic-associated weight gain and diabetes.[469] In a meta-analysis of 33 RCTs (3473 people with SMI), weight control was improved with behavioural interventions compared with control, metformin, anticonvulsive medications topiramate and zonisamide, and adjunctive or antipsychotic switching to aripiprazole (meta-analysis not possible). Evidence was insufficient for all other interventions and for effects on glucose and lipid control.[470]

7.5.3. Smoking cessation

Smoking cessation strategies for persons with SMI are similar to the general population as summarized previously (*Section 6.3.10*), including appropriate pharmacological therapy in combination with behavioural therapy. Brief behavioural interventions (motivational enhancement, personalized feedback) have increased rates of pursuing nicotine dependence treatment compared with psycho-education in people with schizophrenia.[471] Studies have confirmed the safety and efficacy of first-line smoking cessation pharmacotherapies, including varenicline, bupropion, nicotine replacement therapy, and nicotine patch monotherapy in individuals with and without schizophrenia or schizoaffective disorders.[384,472–474] Although studies do not indicate a serious safety signal with varenicline or bupropion, there is a general risk of deteriorated mental health in association with smoking cessation due to nicotine abstinence. People with previous mental health issues should be well informed and followed up carefully during smoking cessation interventions.

Maintenance of pharmacotherapeutic and behavioural treatment has been reported to significantly reduce relapse rates among smokers with schizophrenia.[471] Smoking cessation has a double benefit effect as it also potentially enables the need for a lower dose of antipsychotic treatment. Specifically, smoking can influence the efficacy of multiple medications used in the treatment of SMI through CYP1A2 induction, reducing plasma levels of some drugs (Supplementary data online, *Table S10*). Therefore, smoking cessation may lead to increased plasma levels of these drugs (e.g. clozapine) and thus doses of medications may need to be reduced when someone stops smoking, in consultation with psychiatrist.

7.5.4. Pharmacological management

Psychiatric medication in people with SMI is prescribed long term with a variety of psychotropic medications, depending largely on the state of the disease and comorbidities. People with schizophrenia, other psychotic disorders, and bipolar disorders are treated with antipsychotics, sometimes in combination with antidepressants, mood stabilizers, and frequently anxiolytics or sedatives. The same is true for severe recurrent depression, where antipsychotics are added to antidepressants. CYP450 pharmacokinetic profiles of psychotropic medications can be found in Supplementary data online, *Table S10*.

While pharmacologic treatment in SMI is associated with decreased risk of CVD compared with no treatment, a rational pharmacotherapy is needed as some medications are associated with CV risks. As discussed in *Section 7.6* these include the development of CV side effects via receptor blockade of muscarinic receptors and adrenergic receptors and worsening modifiable CV risk factors.[475]

Rational pharmacotherapy for persons with SMI takes a multifactorial approach as outlined in the principles below:

- Use of monotherapy whenever possible.
- Use of medication with lower propensity to induce or worsen CV risk.
- Addition of medication to prevent CV risk factors (e.g. metformin or glucagon-like peptide-1 receptor agonists to prevent weight gain).
- Consideration of possible drug interactions and monitoring for CV side effects upon initiation of a new drug.
- Ensuring adequate adherence to psychiatric medication.

People with SMI respond to the same strategies to increase adherence as those without SMI, including simplifying medication regimens and use of behavioural interventions. Text message reminders, phone calls, electronic pill counters, and training family members can improve medication adherence in SMI populations.[422]

7.6. Management of cardiovascular conditions in people with severe mental illness

Managing CVD in people with SMI requires good communication and collaboration between mental health and CV specialists. Several factors that may help improve CVD management and secondary prevention in those with CV conditions are listed below and summarized in *Figure 13*.

- Raise awareness of specialists and primary care professionals regarding the importance of controlling CV risk factors.
- Promote adherence to psychotropic drugs; long-acting injectables may help.
- Decrease the number of psychotropic drugs if possible.
- Switch to drugs with less propensity to induce metabolic syndrome, in consultation with psychiatrists and evaluation of relapse risk.[476]
- Reinforce lifestyle modifications and prescribe CV prevention medications as needed.
- Addition of varenicline/bupropion or other forms of nicotine replacement therapy combined with smoking cessation programmes in case of smoking.

7.6.1. Rhythm disturbances

People with SMI are at increased risk of developing supraventricular and ventricular arrhythmias, which may eventually lead to SCD. This increased arrhythmia risk is multifactorial, including distress resulting from the SMI, high prevalence of risk factors and unhealthy lifestyles, CV comorbidities commonly observed in SMI, and side effects of psychotropic medications. Furthermore, autonomic dysfunction, chronic inflammation, and oxidative stress are common in SMI and have been associated with an increased arrhythmia risk.[423]

- Pre-existing arrhythmias or their development after the initiation of treatment can pose significant challenges to the medical management

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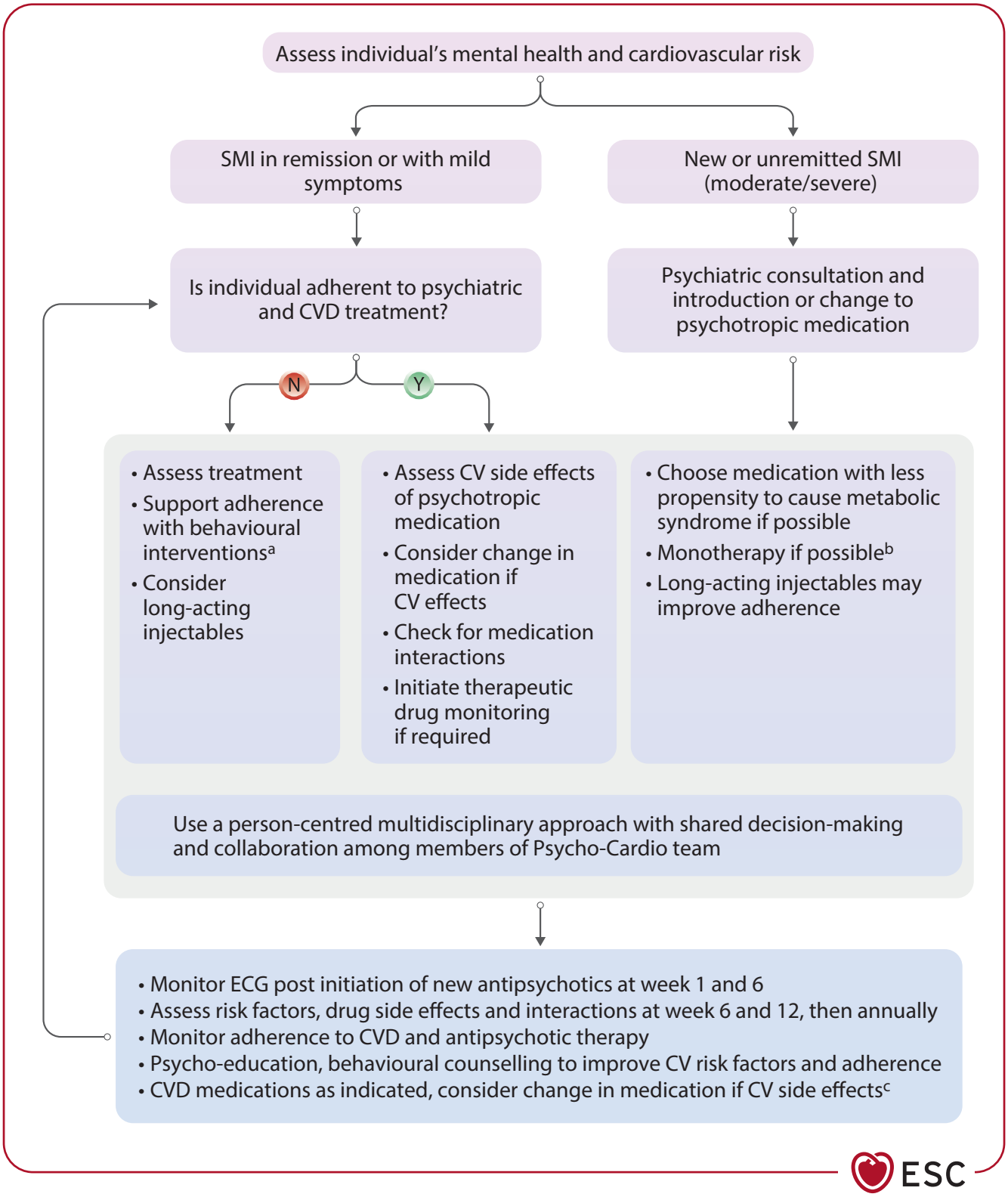
Assess individual's mental health and cardiovascular risk
SMI in remission or with mild symptoms
New or unremitted SMI (moderate/severe)
Is individual adherent to psychiatric and CVD treatment?
Psychiatric consultation and introduction or change to psychotropic medication
N
Y
• Assess treatment
• Support adherence with behavioural interventions[a]
• Consider long-acting injectables
• Assess CV side effects of psychotropic medication
• Consider change in medication if CV effects
• Check for medication interactions
• Initiate therapeutic drug monitoring if required
• Choose medication with less propensity to cause metabolic syndrome if possible
• Monotherapy if possible[b]
• Long-acting injectables may improve adherence
Use a person-centred multidisciplinary approach with shared decision-making and collaboration among members of Psycho-Cardio team
• Monitor ECG post initiation of new antipsychotics at week 1 and 6
• Assess risk factors, drug side effects and interactions at week 6 and 12, then annually
• Monitor adherence to CVD and antipsychotic therapy
• Psycho-education, behavioural counselling to improve CV risk factors and adherence
• CVD medications as indicated, consider change in medication if CV side effects[c]
ESC

Figure 13 Management of people with cardiovascular disease and severe mental illness. CV, cardiovascular; CVD, cardiovascular disease; ECG, electrocardiogram; GLP-1 RA, glucagon-like peptide-1 receptor agonist; SGLT-2i, sodium–glucose co-transporter-2 inhibitor; SMI, severe mental illness. [a]Varenicline or bupropion can be used to support smoking cessation behavioural interventions. [b]Monotherapy for SMI if possible; antipsychotics with lower propensity to worsen CVD risk (psychiatrist to advise). → choice based on severity of symptoms, risk of relapse, medication interactions, comorbidities, and person-centred/shared decision-making preferences. [c]GLP-1 RA and SGLT-2i for diabetes; Metformin first line for antipsychotic associated weight gain.

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of SMI. The risk of SCD is significantly increased in people with SMI with estimates suggesting a two- to four-fold higher risk compared with the general population.[298] Several medications prescribed to persons with SMI have potential pro-arrhythmic side effects and may cause or exacerbate atrial and ventricular tachycardia. Caution and careful monitoring are needed when prescribing potentially pro-arrhythmic drugs in people with known heart disease, with the following considerations: quetiapine, olanzapine, risperidone, iloperidone, ziprasidone, amisulpride, and sertindole increase the risk of QTc prolongation compared with placebo.[477]

- Iloperidone, chlorpromazine, loxapine, risperidone, quetiapine, and paliperidone increase the risk of tachycardia compared with placebo.[478]
- Low-potency first-generation antipsychotics and multi-acting receptor-targeted second-generation antipsychotic treatment (specifically clozapine, chlorpromazine, olanzapine, quetiapine, and risperidone) are associated with an increased risk of AF especially in those with hypertension, diabetes, or CAD although evidence is limited.[479]
- Lithium may induce electrocardiographic changes and arrhythmias such as T-wave inversions, sinus bradycardia, sinoatrial block, PR prolongation, incomplete bundle branch block, QTc prolongation, increased QT dispersion, the Brugada electrocardiographic pattern, and ventricular tachyarrhythmias.[480]

The risk of AF appears not to be generally increased among people with SMI after adjustment for sex and age, although this may reflect underdiagnosis of AF and misinterpretation of palpitation symptoms.[423,479,481] In a study from Korea, young adults (20–39 years) diagnosed with mental disorder had a higher risk of incident AF (adjusted HR 1.53, 95% CI 1.44–1.62).[482]

7.6.1.1. QTc interval prolongation

QTc intervals can be prolonged in association with several antipsychotic drugs such as sertindole, amisulpride, ziprasidone, iloperidone, risperidone, olanzapine, and quetiapine.[477] This effect may be more common in women than men due to differences in pharmacokinetic profiles.[483] A prolongation of the QTc interval increases the risk of torsades de pointes tachycardias and SCD. Therefore, a 12-lead ECG should be recorded before and after initiation of antipsychotic drugs and further ECG controls performed on a yearly basis during long-term follow-up.

Prolonged QTc in response to antipsychotic medication may indicate acquired long QT syndrome and/or reveal an underlying genetic predisposition. Diagnosis and management of long QT syndrome in SMI should follow general Guidelines.[484]

- Acquired long QT syndrome is usually defined by a QTc of >500 ms or a drug-induced change from baseline >60–70 ms.[485]
- In people with QTc intervals >500 ms, suspected causal drugs should be stopped and switched to alternative medication with lower QT-prolonging properties and be evaluated by a cardiologist for underlying genetic conditions.
- In cases of intermediate QTc prolongation (e.g. ≥470 ms in men; ≥480 ms in women), dose reduction or switching to a different antipsychotic may be considered and repeated ECGs should be documented. Individualized risk-benefit assessments are useful, considering the presence of additional risk factors for QT prolongation, symptoms, and the QT-prolonging potential of the prescribed medication.
- Given that QT-prolonging effects are dose dependent, always aim for the lowest effective dose. Interactions with other QT-prolonging drugs like amiodarone, sotalol, or erythromycin should be avoided.
- The inherent risk of QT prolongation associated with specific drugs is provided on the CredibleMeds website.[486]
- QT prolongation may also be the effect of other reversible causes such as hypokalaemia, hypothyroidism, or bradycardia.
- Sinus tachycardia is common in SMI, heart rate correction of the QT interval with the Fridericia formula is optimal, rather than Bazett's formula which overestimates QT at higher heart rates.[487]
- The measurement of QT intervals can be complicated by abnormal T-wave morphology requiring expert consultation for correct interpretation.[477,483]

7.6.1.2. Heart rate changes

Both tachycardia and bradycardia are side effects of antipsychotic medication.[478] Sinus tachycardia has been reported with most antipsychotic medications, including first- and second-generation therapies. It is most common with clozapine (17%–33%),[488] but has usually a transient and benign course. However, possible medical causes of sinus tachycardia should be excluded. In those with symptoms, rate control with cardioselective beta-blockers, calcium channel blockers, or ivabradine may be used. Persistent heart rates above 130 beats per minute (b.p.m) may in rare cases cause a tachycardiomyopathy, which is usually reversible by improved rate control.

Bradycardia is a rare side effect of antipsychotics, with incidence not significantly higher compared with controls.[478] Bradycardia warrants careful clinical attention in people at risk, e.g. in those with pre-existing conduction disturbances or symptoms like dizziness or syncope.

Lithium has a unique mechanism of action and a narrow therapeutic window. Common side effects include sinus node dysfunction, bradycardia, conduction delays (e.g. atrioventricular block, bundle branch block) but also precordial T-wave changes including Brugada pattern, and QT prolongation. Prolonged use and high blood levels increase the complication risk making maintenance of optimal lithium serum levels essential.[480] Since lithium concentration is affected by sodium, conditions like dehydration or renal failure must be managed carefully. However, with appropriate monitoring, lithium does not pose a significant CV risk.[478,480]

In summary, in people with SMI and arrhythmias, it is necessary to evaluate the link between arrhythmias and antipsychotics. If clinically suspected, switching to other drugs with less propensity to cause changes in heart rhythm may be appropriate, however, this must be balanced against the risk of SMI relapse. Clozapine, as the only medication indicated in people with treatment-resistant schizophrenia, is often hard to switch due to a high risk of relapse. A decision algorithm is given in *Figure 14* and additional information is provided in *Table 7*.

7.6.2. Clozapine-induced myocarditis

Although clozapine has been associated with an increased risk of developing myocarditis and cardiomyopathy, reviews and meta-analyses show that event rates and death rates are low. Results are limited by inconsistency in the diagnostic criteria for myocarditis and cardiomyopathy.[489] The odds of clozapine-induced myocarditis increased with concurrent sodium valproate use, and possibly increasing age and higher clozapine dose.[490]

If clozapine-induced myocarditis or cardiomyopathy is suspected, treatment should be discontinued promptly and referred urgently to a cardiologist for diagnostic evaluation.[491] People who have persistent tachycardia at rest, especially during the first 2 months of treatment, should be closely observed for other signs or symptoms of myocarditis or cardiomyopathy (palpitations, arrhythmias, symptoms mimicking MI, chest pain, and other unexplained symptoms of HF). However, specialist advice and link with psychiatrists is needed to prevent inappropriate discontinuation of clozapine.

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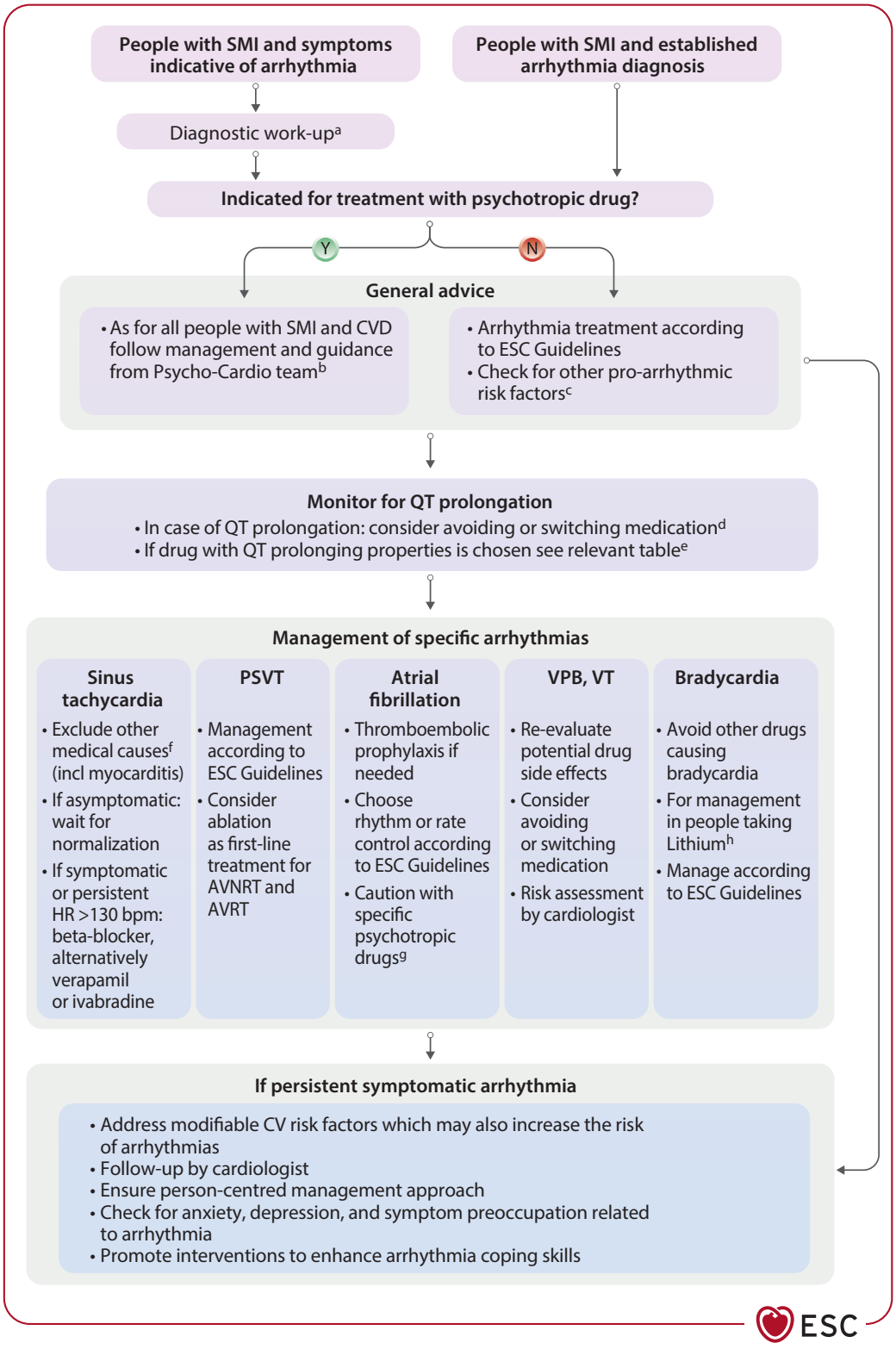
People with SMI and symptoms indicative of arrhythmia
People with SMI and established arrhythmia diagnosis
Diagnostic work-up[a]
Indicated for treatment with psychotropic drug?
Y
N
General advice
• As for all people with SMI and CVD follow management and guidance from Psycho-Cardio team[b]
• Arrhythmia treatment according to ESC Guidelines
• Check for other pro-arrhythmic risk factors[c]
Monitor for QT prolongation
• In case of QT prolongation: consider avoiding or switching medication[d]
• If drug with QT prolonging properties is chosen see relevant table[e]
Management of specific arrhythmias
Sinus tachycardia
• Exclude other medical causes[f] (incl myocarditis)
• If asymptomatic: wait for normalization
• If symptomatic or persistent HR >130 bpm: beta-blocker, alternatively verapamil or ivabradine
PSVT
• Management according to ESC Guidelines
• Consider ablation as first-line treatment for AVNRT and AVRT
Atrial fibrillation
• Thromboembolic prophylaxis if needed
• Choose rhythm or rate control according to ESC Guidelines
• Caution with specific psychotropic drugs[g]
VPB, VT
• Re-evaluate potential drug side effects
• Consider avoiding or switching medication
• Risk assessment by cardiologist
Bradycardia
• Avoid other drugs causing bradycardia
• For management in people taking Lithium[h]
• Manage according to ESC Guidelines
If persistent symptomatic arrhythmia
• Address modifiable CV risk factors which may also increase the risk of arrhythmias
• Follow-up by cardiologist
• Ensure person-centred management approach
• Check for anxiety, depression, and symptom preoccupation related to arrhythmia
• Promote interventions to enhance arrhythmia coping skills
ESC

Figure 14 Management of people with severe mental illness and arrhythmias. AVNRT, atrioventricular nodal reentry tachycardia; AVRT, atrioventricular reentry tachycardia via accessory pathway; bpm, beats per minute; CV, cardiovascular; CVD, cardiovascular disease; ECG, electrocardiogram; ESC, European Society of Cardiology; HR, heart rate; PSVT, paroxysmal supraventricular tachycardia; SMI, severe mental illness; VPB, ventricular premature beat; VT, ventricular tachycardia. [a]History, symptoms, status, 12-lead ECG, Holter-ECG and/or event recorder, echocardiography, blood test and other evaluation if appropriate. [b]See *Figure 13*. [c]Such as hypertension, heart failure, ischaemic heart disease, electrolyte imbalance, history of arrhythmia, or syncope, family history of sudden cardiac death. [d]Special caution with quetiapine, olanzapine, risperidone, iloperidone, amisulpride, sertindole. [e]See *Table 7*. [f]Such as anaemia, hyperthyroidism, infection/sepsis, pain. [g]Special caution with clozapine, chlorpromazine, olanzapine, quetiapine, risperidone. [h]See *Section 7.6.1*.

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Table 7 Management of psychotropic drugs with QT interval prolongation properties

Action	Supporting information
Assess symptoms	Typically, asymptomatic In case of torsades de pointes: palpitations, dizziness, syncope, cardiac arrest.
Diagnostic work-up	• 12-lead ECG providing QTc at baseline and after 1, 6, and 12 weeks after initiating drug • ECG more often in case of QT prolongation • Use Fridericia formula for heart rate correction if there is tachycardia • Check electrolytes: potassium, calcium, magnesium • Ambulatory ECG monitoring in people with symptoms • Exclude possible inherited long QT syndrome.
Management	Special caution with: sertindole, amisulpride, ziprasidone, iloperidone, risperidone, olanzapine, and quetiapine • Always aim for the lowest effective dose • Check for other QT-prolonging drugs • Check for drug interactions • Always special caution when new medication is started • Consult https://www.crediblemeds.org/ for specific information on QT-prolonging drug effects • Correct electrolyte imbalances • Address other reversible QT-prolonging factors (e.g. bradycardia, hypothyroidism, starvation/eating disorders, alcohol and substance abuse, myocardial ischaemia) Note other non-reversible potentially QT-prolonging factors: heart failure, ventricular hypertrophy, recent conversion from atrial fibrillation, impaired hepatic/renal function, female sex, age over 65 years If QTc is prolonged (>470 ms) at baseline, treatment initiation is generally not recommended and should be carefully considered based on individualized risk-benefit assessment (Psycho-Cardio team)[a].
Special precautions	Stop treatment with antipsychotic drug (and any other potentially QT-prolonging medication) if: • QTc >500 ms[b] • Increase in QTc >60–70 ms from baseline[c].

ECG, electrocardiogram; QTc, corrected QT interval.
[a]QTc prolongation (>470 ms) during treatment warrants repeated ECG documentation and thorough evaluation of symptoms and additional risk factors for QT prolongation. Dose reduction or switching to a different antipsychotic drug may be considered in selected cases after individualized risk-benefit assessment (Psycho-Cardio team).
[b]Request urgent consultation with Psycho-Cardio team/cardiologist.
[c]Request urgent consultation with Psycho-Cardio team/cardiologist, repeat ECG.

7.7. Interventions to improve the management of people with severe mental illness and cardiovascular disease

Existing programmes of prevention, early detection, and treatment of CVD have not consistently and significantly improved the CV risk profile in people with schizophrenia and other SMI conditions.[492] Poor motivation, lack of insight and cognitive impairment, and limited participation in decision-making by persons with SMI may be contributing to non-adherence to prevention, diagnostic, and treatment programmes. Cardiovascular disease prevention and treatment programmes need to work with mental health experts to provide CVD screening and care that is accessible and appropriate for people with SMI.

7.8. Section summary points and management consensus statements from *Section 7*

SECTION SUMMARY POINTS

(i) The presence of SMI increases CV risk, especially in younger people.
(ii) Regular CV risk assessment is essential in people with SMI regardless of age, to prevent the development or progression of CVD, ideally before the prescription of antipsychotics and, afterwards, periodically in all stages of illness.
(iii) Management of CVD in people with SMI aims to reduce modifiable CV risk factors, including weight gain, diabetes, hypertension, dyslipidaemia, smoking, unhealthy diet, and sedentary lifestyle habits.
(iv) CVD management in people with SMI benefits from optimizing SMI pharmacotherapy: (i) preferring monotherapy, (ii) using medications less likely to induce weight gain or other CV risks, (iii) monitoring for possible drug interactions and side effects, and (iv) ensuring medication adherence.
(v) Efforts to alleviate the impact of psychosocial and stress-related factors are needed in people with SMI.

MANAGEMENT CONSENSUS STATEMENTS

(i) Addressing stigma and managing CVD in people with SMI in accordance with CV Guidelines and best clinical practice is a responsibility of all healthcare professionals.
(ii) CV care for people with SMI can be improved by following a holistic person-centred approach, involving close collaboration between the Psycho-Cardio team with psychiatrists, general practitioners, and sometimes other specialists to proactively facilitate the engagement of people with SMI in such programmes.

Continued

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8. Mental health in specific populations and situations

8.1. Sex and gender differences in mental health and cardiovascular disease

Biological ('sex') and sociocultural ('gender') aspects may explain differences or disparities between women and men in incidence, prevalence, presentation, diagnosis, management, and response to treatment in CV and mental health conditions (*Figure 15*). Sex reflects biological factors like genetics, anatomy, physiology, and hormones, while gender involves socially constructed norms shaping roles, relationships, and power dynamics. Gender interacts with sex, affecting traits that define women, men, and intersex individuals. Pregnancy and menopause are clear examples of the differential influence of sex and gender in CV and mental well-being. Multiple studies and analyses have shown that:

- Depression and anxiety are twice as prevalent in women, have increased more in women over the past two decades compared with men, and are important risk factors for ACS and CV mortality.[94,493–495]
- Risk ratio for psychosocial factors is higher in women with CVD compared with men with CVD (RR 25.7 vs 21.7, respectively).[56,496]
- The association between depression or anxiety and CVD risk is stronger in young and middle-aged women compared with men.[94,497]
- Women experience a greater impact from chronic self-perceived stress and marital stress, whilst men are more affected by job-related stress.[498]

However, this has to be interpreted in the context of the following factors: (i) prevailing social norms may lead to underreporting of mental stress in men,[499,500] and (ii) men may have better perceived health and less anxiety than women, despite reporting more health risk behaviours.[501]

Sex differences in stress response have been seen in animal and human models.[502,503] Although pre-clinical studies in rodents and neurobiological studies in the past have predominantly been done in males, evidence of sex differences in neurobiological alterations in people with depression and anxiety is mounting.[504–507] These are associated with genetic differences, inflammation, platelet activation, sympathetic function, and hormone-related receptor signalling pathways.

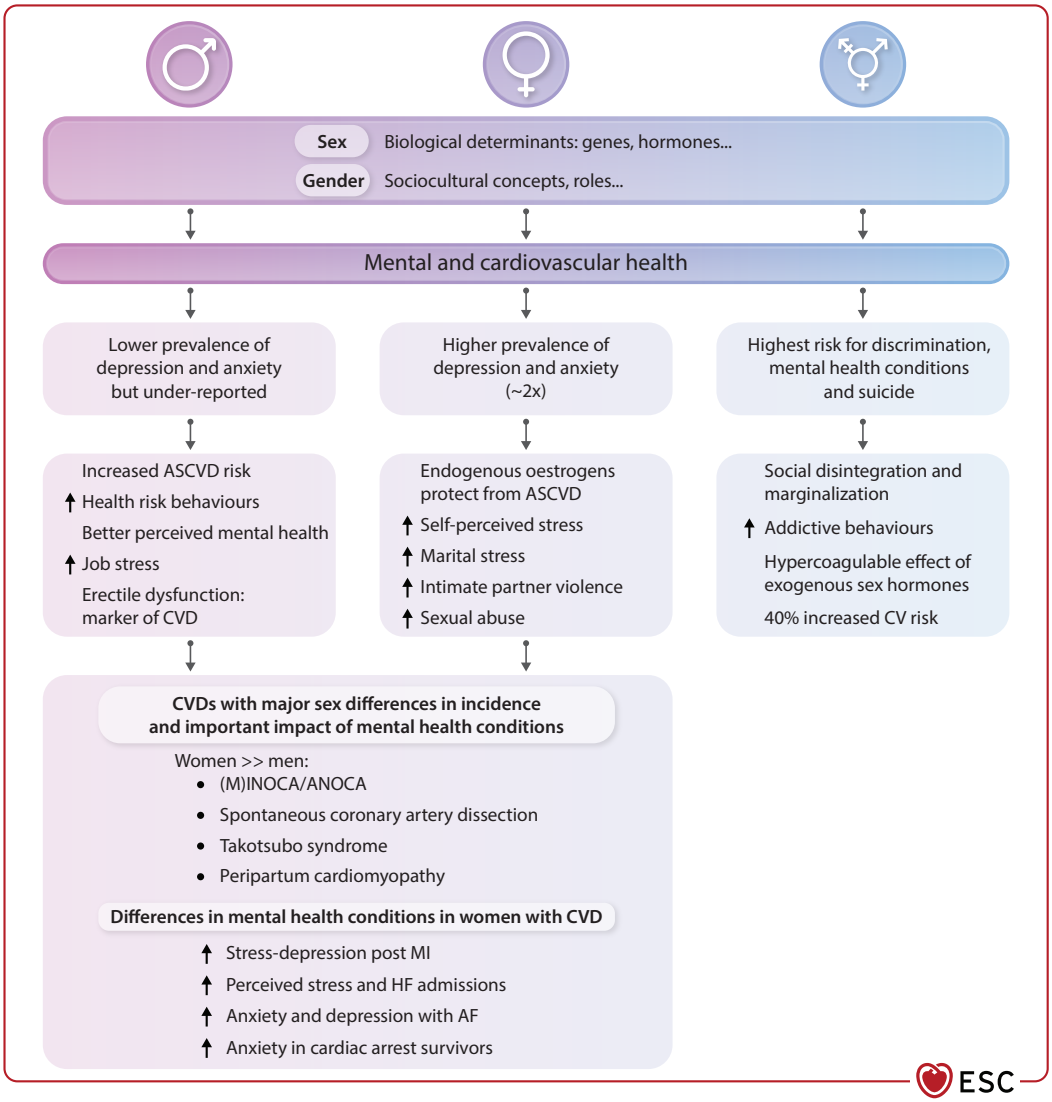
Sex
Biological determinants: genes, hormones...
Gender
Sociocultural concepts, roles...
Mental and cardiovascular health
Lower prevalence of depression and anxiety but under-reported
Higher prevalence of depression and anxiety (~2x)
Highest risk for discrimination, mental health conditions and suicide
Increased ASCVD risk
Health risk behaviours
Better perceived mental health
Job stress
Erectile dysfunction: marker of CVD
Endogenous oestrogens protect from ASCVD
Self-perceived stress
Marital stress
Intimate partner violence
Sexual abuse
Social disintegration and marginalization
Addictive behaviours
Hypercoagulable effect of exogenous sex hormones
40% increased CV risk
CVDs with major sex differences in incidence and important impact of mental health conditions
Women >> men:
(M)INOCA/ANOCA
Spontaneous coronary artery dissection
Takotsubo syndrome
Peripartum cardiomyopathy
Differences in mental health conditions in women with CVD
Stress-depression post MI
Perceived stress and HF admissions
Anxiety and depression with AF
Anxiety in cardiac arrest survivors
ESC

Figure 15 Sex and gender differences in the psycho-cardio interaction. AF, atrial fibrillation; ANOCA, angina with non-obstructive coronary arteries; ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular; CVD, cardiovascular disease; HF, heart failure; MI, myocardial infarction; (M)INOCA, (myocardial infarction) ischaemia with non-obstructive coronary arteries.

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Some SES factors like educational level and sex-specific life events (i.e. pregnancy, sexual abuse, intimate partner violence), have a different impact on the stress response in women and men. Women have a higher inflammatory response to stress compared with men, which is associated with future adverse CV outcomes in people with IHD.[508] The association between menopause transition and depression remains contentious, although severe vasomotor symptoms are recognized as a contributing factor associated with depression.[509,510] Hormonal changes during menopause transition frequently induce mood disturbances, adversely impacting QoL and work performance.[511,512] During peri-menopause but not in post-menopause, temporary hormone therapy may alleviate these symptoms.[511,512]

In men, erectile dysfunction has not only been shown to be a consequence of CVD, it is also a risk marker for future CVD.[513] A recent meta-analysis demonstrated that sexual dysfunction is also a predictor of future CVD in women.[514]

8.1.1. Cardiovascular disease and mental health conditions in transgender individuals

Transgender individuals show a significantly higher risk for mental health conditions, including suicidality, social disintegration, and marginalization, compared with non-transgender individuals.[515] High rates of discrimination and low levels of social support predispose to addictive behaviours in transgender persons,[516] but insufficient data are available to differentiate between transgender subgroups. Gender-affirming therapy, including sex hormones, aligns individuals with their gender identity, enhancing QoL.[517] The psychosocial benefits of hormone therapy with an improved body image may result in healthier lifestyle choices. Evidence in the ageing transgender population suggests that both transgender men and women face a 40% higher risk of CVD compared with cisgender peers of the same birth sex.[518–521] The hypercoagulable effect of exogenous sex hormones, alongside the increase in traditional CVD risk factors, may mediate this elevated risk.

8.1.2. Sex and gender differences in mental health in people with obstructive coronary artery disease

The impact of a life event like a diagnosis of CVD on mental stress affects all genders. However, long-term population studies evaluating their influence according to sex and gender are scarce. Negative stress leads more often to adverse lifestyle behaviours and substance use in men, whereas sociocultural inequalities, household problems, and ACEs more often negatively affect women with CVD.[522] Countries with the highest levels of gender equity have reported some of the greatest reductions in 40 year CVD mortality rates.[496,523]

The negative impact of depression on obstructive CAD in women is relatively more severe in younger women (<55 years) than at older ages.[510,524] Moreover, feminine gender roles, lower educational level, and distress-related psychological factors such as anxiety are important determinants of outcomes after ACS in both sexes.[525] Meta-analyses of negative psychological factors on obstructive CAD found no significant differences among men and women.[106,526] In clinical practice, however, sex and gender differences in heart–brain interactions importantly contribute to different manifestations of stable and unstable IHD.[507,527]

8.1.3. Sex and gender differences in mental health in ischaemia/angina with non-obstructive coronary arteries and coronary vasomotor disorders

Psychological risk factors, including depression and anxiety are prevalent among women with myocardial ischaemia or angina with non-obstructive coronary arteries (INOCA/ANOCA).[56] Mental stress triggers endothelial dysfunction and inflammation.[528–531] While some studies associate anxiety with INOCA/ANOCA, others found no link between depression or general anxiety and these conditions.[532,533] Mental stress-induced ischaemia, more prevalent in women than men, correlates with adverse CV outcomes.[534,535] This may be associated with worse long-term prognosis, particularly in women.[536,537] The influence of mental stress on INOCA/ANOCA contributes to their underdiagnosis and undertreatment in women.[538]

Young women with a history of ACS have a two-fold higher likelihood of developing mental stress-induced myocardial ischaemia compared with men.[535] Chronic mental stress is a significant trigger for spontaneous coronary artery dissection (SCAD), which is nine times more common in women.[539–541] Emotional stressors are reported twice as frequently prior to SCAD-ACS as by other ACS cohorts.[542,543] Since most people experiencing SCAD are relatively young (40–60 years), rehabilitation should prioritize stress management, addressing work-life balance, and other present stressors. Psychological counselling may be needed in selected people.

8.1.4. Sex and gender differences in mental health in people with takotsubo syndrome

Acute stress-induced takotsubo syndrome (TTS) occurs eight–nine times more frequently in women than in men, likely due to different coping strategies for stress.[544] Women over 55 years of age are five times more likely to develop TTS compared with younger women, as risk is linked to increased sympathetic tone after menopause.[545,546] While physical stressors more often affect men, women are more likely to experience an emotional trigger.[547,548] These different triggers suggest two categories of TTS:[549] primary TTS, affecting women after emotional stress with limited left ventricular dysfunction, and TTS triggered by physical stress, which causes more severe left ventricular dysfunction and a worse prognosis. The latter seems to affect women and men equally. A direct connection between the brain and the heart associated with autonomic functions and regulation of the limbic system has been identified.[550] Mental health conditions are common in people with TTS, indicating that combined psychotherapy and ECR could improve mental health and reduce negative thinking more effectively than ECR alone.[350] People with pre-admission psychiatric disorders are at a higher risk of recurrent TTS.[551] The use of SSRIs may help prevent recurrence in selected individuals.[551]

8.1.5. Sex and gender differences in mental health in people with heart failure

Women are underrepresented in most HF trials, leading to a lack of sex- and gender-specific data on the impact of mental health conditions. HF prevalence varies between the sexes: men typically present with HF with reduced ejection fraction following ACS, while women more often experience HF with preserved ejection fraction due to hypertension, obesity, and ageing.[552] Sexual dimorphism is also evident in the expression of hereditary cardiomyopathies and risk factors like breast cancer, and the potential treatment-induced cardiomyopathy. Additionally, there are sex-specific disorders such as peri-partum cardiomyopathy.

Psychological stress has received limited attention as a potential disease modifier in HF. As HF with preserved ejection fraction often remains undiagnosed, this contributes additional stress on the affected predominantly female population. However, qualitative studies support the assertion of non-diagnosis burden.[553,554] The progressive course of HF, with increasing functional limitations, further increases stress in both males and females.

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Higher psychological stress and anxiety worsen HF outcomes.[215,216,555,556] Women with HF, former smokers, those with lower income, and people with obesity report higher perceived stress, as do people with New York Heart Association (NYHA) class II HF, compared with asymptomatic NYHA class I HF.[215,557] Social determinants of health influence HF prevalence, with the highest rates of HF and related readmissions observed in the most economically disadvantaged communities with more representation of women and individuals from ethnically diverse backgrounds.[558]

8.1.6. Sex and gender differences in mental health in people with arrhythmias

In people with AF, anxiety levels are significantly higher in women compared with men, potentially due to older age, living alone (e.g. divorced/widowed), or comorbid conditions.[559] Chronic AF increases anxiety, depression, and affects QoL in both genders, but the effect is more pronounced in women.[560] Depression is more common in women with chronic AF,[561] and affects the subjective burden of symptoms, suggesting that addressing psychological comorbidities may improve symptom management and HRQoL. Anxiety is an important trigger for AF recurrence after cardioversion and ablation therapy.[562]

Women report higher levels of anxiety (general and ICD-related), and higher levels of body image concerns than men when having an ICD.[563] They also express worries about damaging the ICD during breast cancer screening, which in addition may compromise the quality of mammography images.[564]

In a prospective observational study of OHCA survivors, females reported significantly higher symptoms of anxiety and PTSD compared with men, with younger women showing the highest symptom severity. No sex differences were observed for depression.[178] In a cohort of 249 people with ICD,[565] most had relatively low distress scores at baseline (mean anxiety 4.23 ± 4.47; mean depression 5.60 ± 4.73). However, those who received a shock showed a worsening of PTSD symptom severity scores at 3 months (11%), 6 months (7%), and 12 months (7%).

8.1.7. Mental health conditions associated with peri-partum cardiomyopathy

Peri-partum cardiomyopathy is a serious condition with significant consequences for both mother and child, causing substantial psychological and social stress. Mental health conditions, including peri-natal psychiatric illness such as major depression, panic disorder, and PTSD, can worsen prognosis. Screening, diagnosis, and multidisciplinary management of peri-partum cardiomyopathy-associated mental conditions are described in a recent dedicated ESC Heart Failure Association scientific statement.[566]

8.2. Mental and cardiovascular health in older adults

Countries across the globe are experiencing an exponential rise in the proportion of older persons (often defined as aged 60 years or more) in their population, such that the WHO predicts the number of people aged 80 years or older will triple between 2020 and 2050.[567] With ageing populations comes a growing burden of chronic condition management due in part to 'inflammageing', whereby chronically raised blood inflammatory markers increase the risk of morbidity, disability, frailty, and early mortality.[568,569] According to the Global Burden of Disease programme, both CVD and mental health disorders are on the rise.[570,571] In older adults, the prevalence of depression (19.2%), anxiety (16.5%), and stress (13.9%) are already relatively high.[572] However, specific mental health disorders like late-life depression are set to increase,[573] which has implications for CVD management. A recent systematic review and meta-analysis of 61 prospective cohort studies (198 589 older adults) found that late-life depression is associated with increased risk of CV mortality (RR 1.31, 95% CI 1.20–1.43).[574]

Whilst there is reasonable population-level data on individual conditions, the rates of mental health disorders within older adults with any type CVD and vice versa are not well known. Using HF as an exemplar, which is mostly a disease of older adults, it would seem that the global co-occurrence of CVD with mental disorders like depression is significant. One of the largest meta-analyses to date (149 studies, $n = 305\,407$, mean age 65.2 ± 7.1 years) determined that the prevalence of any severity depression in HF was 41.9%, and severe depression was 28.1%.[575] In older adults with AF, a meta-analysis of 26 studies determined the rate of depression as 40.3% and anxiety as 33.6%.[576] Such results suggest that the rates of depression may be significantly higher in older adults with co-existing CVD, compared with the previously described population norms for older adults (19.2% depression, 16.5% anxiety).[572]

Non-pharmacological therapies: given that suboptimal mental and CV health are common in older adults, it is necessary to develop interventions that work synergistically to improve outcomes in both conditions. Unfortunately, very few interventions have been trialled and thus clinical practice evidence is limited. One narrative review of integrated physical-mental healthcare services for older people living with mental health diagnoses (9 studies, $n = 1728$) determined that such interventions improved a range of health outcomes, however, studies were not large nor robust.[577] The majority of RCTs included in the Cochrane systematic review and meta-analysis of psychological interventions discussed in *Section 6*, included older adults with comorbid CVD and mental disorders based on sample age (14 of 21 trials included adults ≥60 years, age range 56 to 71 years). This review suggests that multicomponent psychological interventions such as CBT, MotInt, and mindfulness can improve anxiety and depression in this population, however, it did not improve MACE.[263] A Cochrane review of social network or social support interventions, both of which are postulated to be useful in CVD and mental health conditions, reported that in predominantly older patients with CVD (median age 62.5 years) and comorbidity (including concurrent anxiety and depression), there were no effects on CVD and psychological well-being outcomes.[578]

Pharmacological therapy: managing pharmacological treatments in elderly patients with both mental health disorders and CVD requires careful consideration of dose adjustments and potential drug interactions due to age-related changes in pharmacokinetics and pharmacodynamics. Ageing affects drug absorption, distribution, metabolism, and excretion. Reduced hepatic and renal function can alter drug clearance, necessitating dose adjustments. For instance, lower doses of benzodiazepines, antidepressants, and antipsychotics are often required due to increased sensitivity and risk of adverse effects.[579] Individualized care, considering the patient's overall health status, comorbidities, and personal health goals is needed. Selecting safer drug alternatives, adjusting doses, and vigilant monitoring for adverse effects and interactions while balancing efficacy and safety is advisable. Guidance on potential toxicity and interactions per drug class is further discussed in *Section 6*. A summary focusing specifically on the elderly population follows. SSRIs and SNRIs are generally the preferred antidepressants due to their favourable side effect profiles. ECG monitoring may be needed, especially when combined with other QT-prolonging drugs such as antiarrhythmics. The combination of antipsychotics and antiarrhythmic drugs or other QT-prolonging agents requires careful monitoring.

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Additionally, antipsychotics metabolized by the CYP system can interact with CV drugs like beta-blockers and statins, necessitating dose adjustments.[580,581] Lithium can cause arrhythmias, so it requires regular monitoring of serum levels and renal function. It can interact with diuretics and angiotensin-converting enzyme inhibitors, increasing the risk of lithium toxicity.[582] Benzodiazepines can cause sedation and respiratory depression, especially when combined with other central nervous system depressants.[579,582,583]

Polypharmacy is highly prevalent in elderly patients, increasing the risk of drug interactions. For example, combining central nervous system depressants with CV drugs can lead to additive effects, such as increased sedation or hypotension. Regular medication reviews and deprescribing where appropriate are essential to minimize these risks.[584] Specific interactions with CV drugs need to be specially assessed. For example, antipsychotics can increase the risk of QT prolongation, arrhythmias, or hypotension when combined with beta-blockers or antiarrhythmics.[580,583] Antipsychotics can increase the risk of myalgia, myopathy, or creatine kinase elevation in combination with statins.[580]

8.3. Mental health and cardiovascular disease in people with frailty and multimorbidity

8.3.1. Mental health and frailty

Frailty is a state of diminished physiologic reserve and increased vulnerability to adverse health outcomes.[585] It is a potentially reversible dynamic state fluctuating over time in response to stressors and interventions. Its incidence increases with age and overlaps with multimorbidity.[585,586] Cardiovascular disease and frailty arise from similar causal mechanisms, and each increases the risk of the other condition.[569] Frailty has been found to affect 40%–80% of people with HF,[587] and to have a pooled prevalence of 19% among individuals with IHD.[588] The substantial prevalence of frailty among older adults with CVD and associated risks for adverse events such as falls necessitate increased awareness and evaluation by clinicians.[589]

Most brief screening tools used clinically to assess frailty focus on biomedical domains, rather than including a more holistic approach. Comprehensive geriatric assessments are advised in older adults to assess multiple domains including psychological and socio-environmental contributors to frailty.[585] Depression, anxiety, and frailty are associated with each other as seen in both observational and Mendelian randomization studies, with a bidirectional relationship found between depression and frailty.[590,591] An analysis of 444 094 participants (median follow-up 7.8 years) determined that frailty resulted in over three times the risk for depression and twice the risk for anxiety in adjusted analyses.[592]

8.3.2. Mental health, cardiovascular disease, and multimorbidity

Multimorbidity is defined as the presence of two or more chronic conditions in one person.[593] It is estimated to affect ~40% of the world's population,[594] and incidence is predicted to rise in parallel with gains in life expectancy and trends in global population ageing.[595] At the societal level, multimorbidity is associated with significant healthcare use,[595] and related utilization costs.[596] At the individual level, it results in loss of agency and isolation,[597,598] which in turn can lead to vulnerability, frailty, and a need for social care.[599] When interrogated by disease or disease clusters in population studies,[600] and systematic review,[601] people with multimorbidity appear to have a high burden of concurrent CVD and mental health disorders like depression. However, there is no consensus across multimorbidity cluster studies and results are dependent upon the measure and/or threshold used to define multimorbidity.[602]

The growing burden of multimorbidity and its complexity necessitates collaborative management. Given that CVD and mental health disorders are frequently highlighted as important contributors to multimorbidity, it is reasonable that clinicians working in these fields can and should drive improvements in care. Degenerative neurological diseases should be considered as part of the multimorbidity assessment, but this particular aspect is out of the scope of this document. Within the secondary care setting, the evidence presented in *Section 6.6* is relevant to the management of multimorbidity, and the implementation of the Psycho-Cardio team would likely drive improvements in care and outcomes. However, there is an absence of empirical research conducted in the secondary care setting and trials of bespoke multimorbidity management models are urgently needed. Within the primary care setting, there have been mixed results in RCTs of integrated care models. The largest trial to date (3D: Dimensions of health, Depression, and Drugs) which was conducted on older adults (mean age 71 years) failed to meet its primary or secondary endpoints.[603] A Cochrane review and meta-analysis of interventions designed to improve outcomes in patients with multimorbidity in the primary care or community setting (18 RCTs) reported that there was evidence that such interventions improved mental health outcomes, but there was no or very little impact on clinical, functional, and healthcare use outcomes.[604] Overall, the evidence suggests these interventions are effective for improving mental health outcomes, however, further research is required to identify interventions that have dual effects (i.e. improve mental health and CVD outcomes).

8.3.3. Summary of evidence in older adults with cardiovascular disease and mental disorders

The older adult is at increased risk for the associated conditions of CVD, mental health conditions, multimorbidity, and frailty. These conditions along with polypharmacy increase the complexity of management and require expertise from the Psycho-Cardio team. Comprehensive geriatric assessment can highlight important issues and ensure that psychosocial domains are identified and addressed. The evidence for non-pharmacological interventions and integrated care models in older adults with CVD and mental disorders is heterogeneous. However, based on the current evidence these interventions appear to be effective in improving mental health outcomes, although they are less likely to significantly improve CVD outcomes. A summary of the core issues in the management of older adults with CVD, multimorbidity, and polypharmacy is presented in *Figure 16*.

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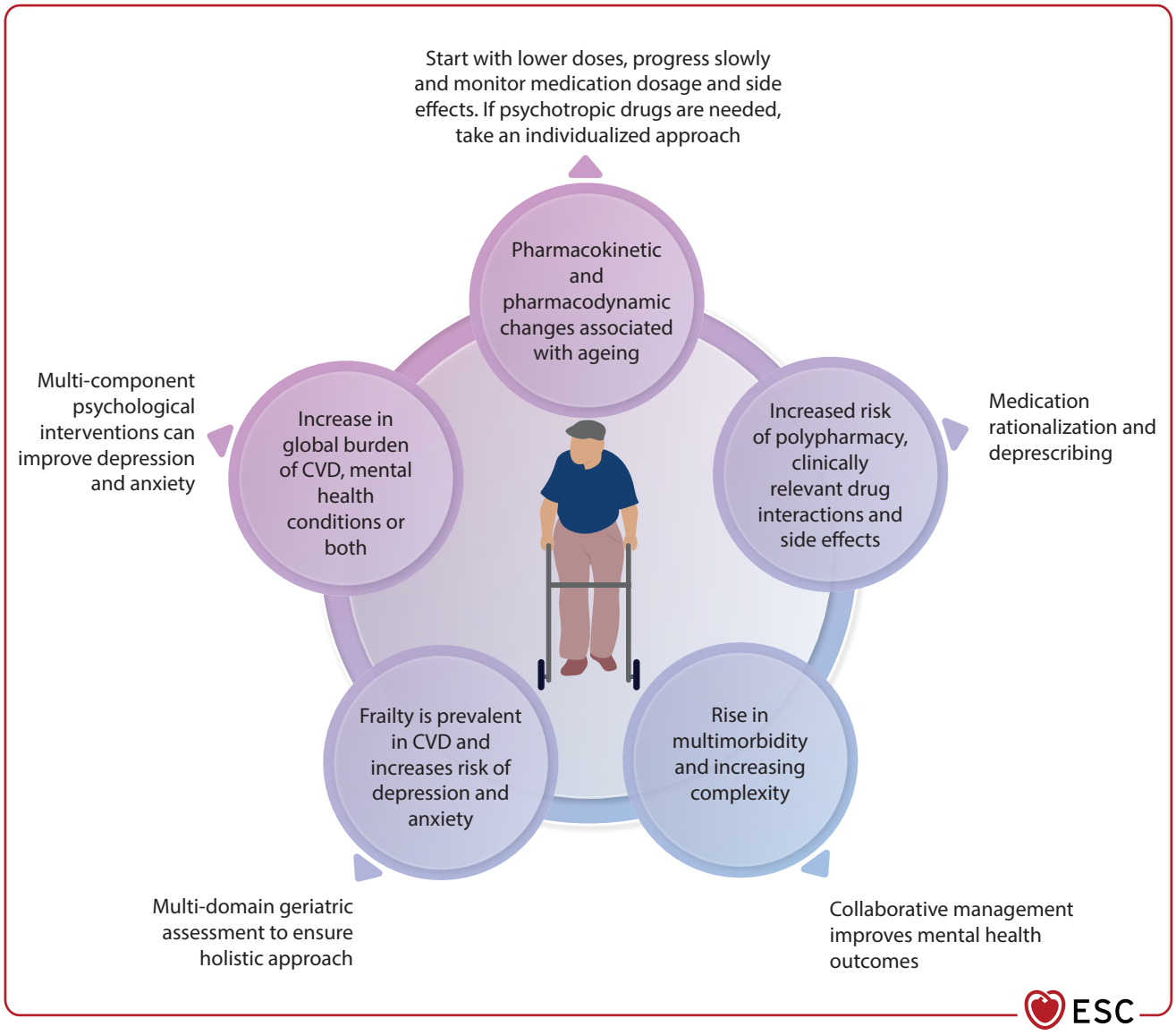
Start with lower doses, progress slowly and monitor medication dosage and side effects. If psychotropic drugs are needed, take an individualized approach
Pharmacokinetic and pharmacodynamic changes associated with ageing
Increased risk of polypharmacy, clinically relevant drug interactions and side effects
Rise in multimorbidity and increasing complexity
Frailty is prevalent in CVD and increases risk of depression and anxiety
Increase in global burden of CVD, mental health conditions or both
Medication rationalization and deprescribing
Collaborative management improves mental health outcomes
Multi-domain geriatric assessment to ensure holistic approach
Multi-component psychological interventions can improve depression and anxiety
ESC

Figure 16 Ageing, mental disorders, and cardiovascular disease. CVD, cardiovascular disease.

8.4. Mental health and cardiovascular disease in socioeconomically deprived populations

Individuals facing economic difficulties often experience increased stress, reduced access to healthcare, and limited opportunities for social engagement.[605] The role of psychosocial stress, its determinants, and impact on mental health and CV risk have been presented in *Section 4*. Psychological stressors linked to socioeconomic deprivation can exacerbate the risk and progression of CV conditions.[606,607] Concerns about financial or housing stability and other basic needs may amplify hormone stress responses, potentially accelerating CVD progression while increasing the vulnerability to mental health conditions like depression and anxiety.[608] Lower SES often correlates with unhealthy lifestyle behaviours, further exacerbating CVD risk. Research has consistently demonstrated that CVD and HF are significantly more prevalent among individuals with low SES, with disparities more pronounced in marginalized communities, where structural inequalities amplify the impact of socioeconomic deprivation on health outcomes.[607,609] Socioeconomic deprivation status seems to be an important covariate in CV risk estimation models while risk scores that exclude socioeconomic deprivation under- and overestimate risk in the most and least deprived individuals, respectively.[606]

Mental health conditions following CVD events are more common in individuals with lower SES. Mental health service utilization following an MI is more frequent among men and women living in areas with high ethnic concentration and material deprivation.[610] Several factors have been postulated as potential mechanisms linking lower SES and higher risk of mental health conditions and CVD (*Figure 17*).

Health inequities are also more frequent among populations such as the homeless, individuals with substance use disorders, sex workers, and imprisoned individuals with the impact of exclusion being greater in females than in males.[611] While addressing socioeconomic deprivation is beyond the scope of practice, it is reasonable for healthcare professionals to:

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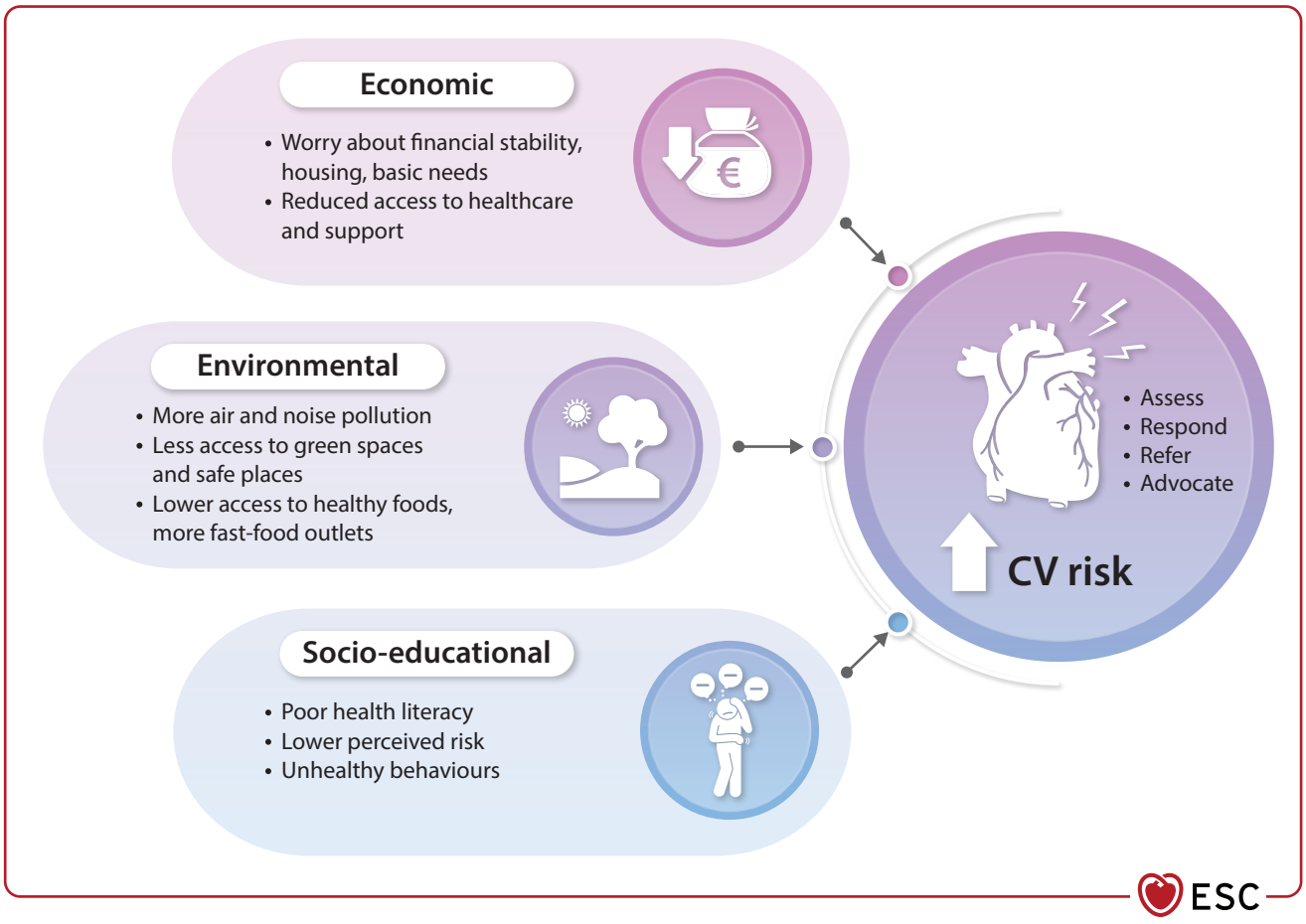

Figure 17 Mechanisms through which socioeconomic deprivation contributes to cardiovascular risk. CV, cardiovascular.

- Recognize that people facing socioeconomic deprivation may have increased risk of CVD and mental health conditions and may struggle to make healthy lifestyle changes.
- Tailor lifestyle advice and behaviour change strategies to the specific challenges of individuals living in deprived areas.
- Support policies and governmental action that ensure equitable access to physical and mental healthcare, healthy food, exercise, and safe places for walking.
- Advocate for efforts to reduce environmental pollution.

8.4.1. Mental health and cardiovascular disease in migrants and refugees

Minority populations are often subject to discrimination, socioeconomic disadvantage, and inequity of access to optimal clinical care.[612,613] Migrants and refugees, as vulnerable groups, are at increased risk of mental health conditions and disorders, often with greater prevalence of CV risk factors and socioeconomic deprivation.[614] Migrants in particular experience higher rates of CVD morbidity and mortality than host populations.[615] War refugees are also at higher risk for CVD and mental health conditions, especially PTSD, though they present lower risk of suicide.[613] Additionally, migrants and refugees often encounter language and cultural barriers, making engagement with community leaders essential for improving communication in cross-cultural consultations in healthcare.[616] While stakeholders' involvement can reduce healthcare barriers, structural factors may limit the scope and sustainability of these improvements in practice.[617]

Mental health challenges in migrant populations are illustrated in *Figure 18*.

Healthcare professionals can support migrant groups with CVD and mental health conditions by:

- Adopting culturally sensitive approaches.
- Collaborating with community stakeholders.
- Tailoring community-based strategies to different ethnic groups.

8.4.2. Barriers to mental healthcare access

Socioeconomic deprivation creates significant barriers to accessing both mental healthcare and CV care for individuals with CVD, worsening the challenges faced by this vulnerable group. Financial constraints, lack of insurance coverage, and transportation difficulties are major obstacles, with stigma surrounding mental health further exacerbating the problem. Despite high rates of depression and anxiety in this population, the utilization of mental health services remains low due to these barriers.[606,618–624]

Comprehensive strategies are needed to overcome these barriers and ensure equitable access to healthcare, including subsidizing mental health services, expanding insurance coverage, integrating mental healthcare into primary care settings, and investing in telehealth. High costs of therapy, medication, and other interventions can be prohibitive, deterring people with CVD from seeking needed care, with the financial burden of CVD care further limiting resources for mental health support.[619]

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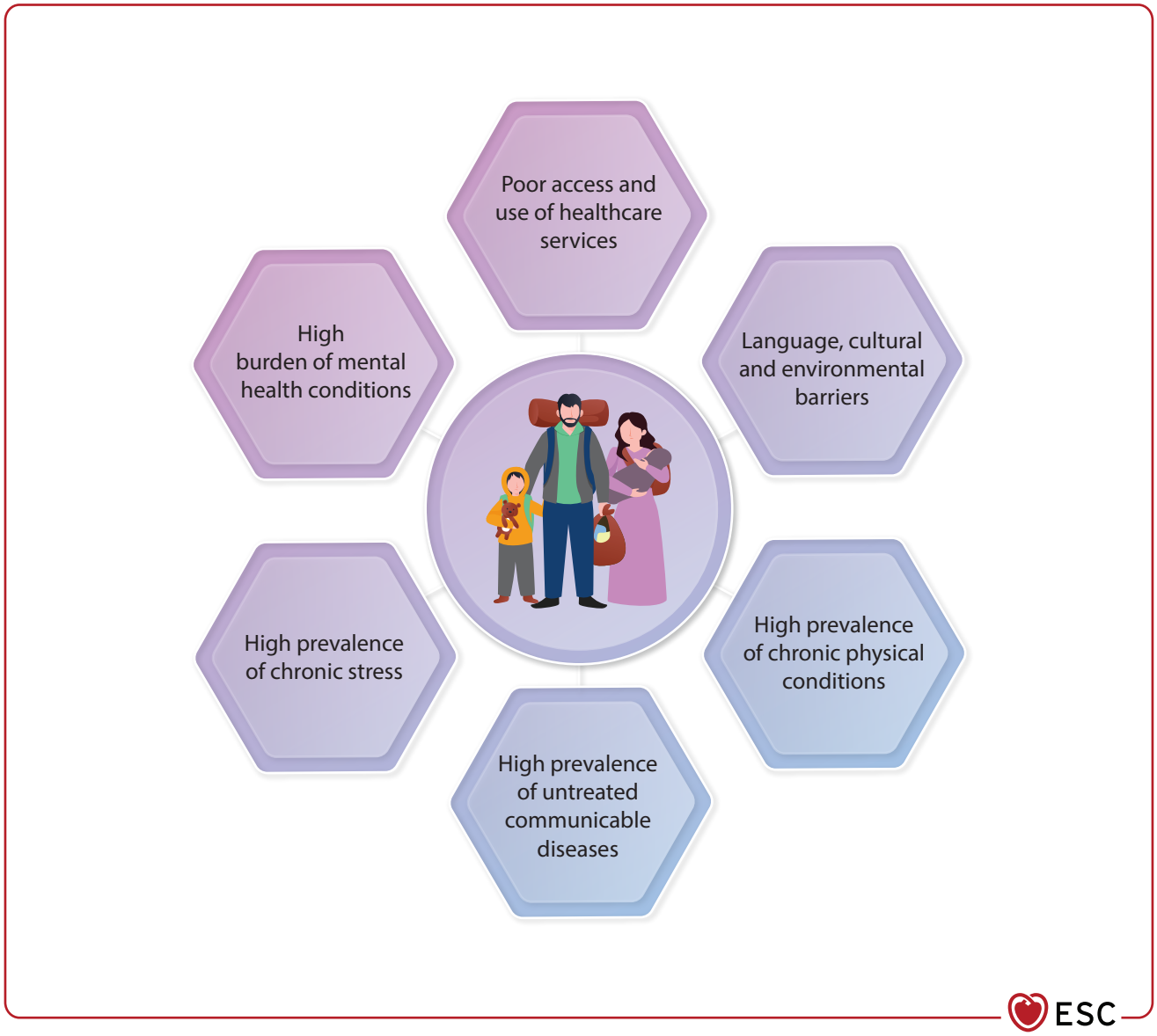
Poor access and use of healthcare services
Language, cultural and environmental barriers
High prevalence of chronic physical conditions
High prevalence of untreated communicable diseases
High prevalence of chronic stress
High burden of mental health conditions
ESC

Figure 18 Mental health challenges in migrant populations.

Additionally, the lack of comprehensive health insurance coverage is a significant issue, with many socioeconomically disadvantaged individuals unable to afford out-of-pocket mental health services. This further perpetuates disparities in access to necessary mental healthcare.[620] Addressing these challenges through enhanced service provision and support is essential for improving mental health outcomes in people with CVD from socioeconomically deprived backgrounds.

8.4.3. Stigma in healthcare provision

Mental health-related stigma is a major barrier to accessing healthcare, operating at three interconnected levels: structural, interpersonal, and intrapersonal.[625] Structural discrimination is reflected in the disparity between physical and mental healthcare provision, resulting in limited and poor-quality mental health services.[626] Interpersonal stigma involves problems of knowledge (ignorance), attitudes (prejudice), and behaviour (discrimination). Intrapersonal mental health stigma, or self-stigma, reduces help-seeking behaviour and further contributes to health disparities.[627]

Stigma affects all populations across different socioeconomic strata, contributing to mental health disparities. Effective interventions to reduce stigma include social contact with individuals with mental health disorders and personal relationships, such as with friends or family members. Educational interventions, especially for general healthcare professionals with little or no formal mental health training, have shown promise in decreasing stigma.[626] However, there is a significant research gap regarding effective interventions to prevent and combat structural and interpersonal stigma. Enhancing education to include training on mental health and stigma for healthcare professionals could be crucial in addressing these issues.

8.4.4. Community and policy interventions

Community-level and policy interventions are essential to reduce the adverse impact of socioeconomic deprivation on mental health in individuals with and without CVD.[607,628,629] Initiatives addressing disparities include:

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- Ensuring access to quality health education for socioeconomically disadvantaged individuals to improve mental and CV outcomes.
- Creating job opportunities and implementing affordable housing initiatives and ensuring equitable access to healthcare services to address mental health needs,
- Improving access to healthy foods and safe spaces for physical activity to reduce CVD risk.
- Ensuring equitable access to healthcare services to address mental and CV health needs.
- Integrating successful interventions into broader health systems and social policies to enhance mental and CV health support.[630–637]

8.5. Mental health and cardiovascular disease in people with cancer (cardio-oncology)

8.5.1. Mental health in people with cancer and cardiovascular disease

Chronic stress may contribute to cancer development.[638] Cancer diagnosis and treatment initiation may cause or intensify psychological distress,[639] leading to an increased risk of major CV events (HF, ischaemic stroke, ACS, AF), with the highest incidence appearing 6–12 months after cancer diagnosis.[640–642] People with a new diagnosis of cancer experience significant stress and anxiety associated with an uncertain prognosis, which may even trigger suicidal ideations. In prostate cancer, the risk of CV death was increased during the first month after diagnosis (~two-fold) and highest in people with metastatic cancer (~three-fold).[642] New CV symptoms (e.g. venous thrombosis, pulmonary embolism, stroke, MI, TTS, arrhythmia) may appear with cancer,[643] suggesting common underlying factors, such as chronic inflammation and thromboembolic disorders. However, the importance of stress may be crucial.

Takotsubo syndrome in people living with cancer is a notable example of a role of stress and anxiety in cardio-oncology.[644–647] Three of the most important independent prognostic predictors of mortality in people with TTS include cancer history (HR 2.004; $P = .004$), physical stress as a trigger (HR 1.882; $P = .012$), and history of depression (HR 1.622; $P = .009$).[648] Takotsubo syndrome in people with prior intrathoracic malignancies and radiation therapy carries a higher risk of cardiogenic shock, cardiac arrest, arrhythmia, stroke, respiratory failure, and all-cause mortality.[649]

People with cancer and concomitant CVD may fear that their CVD will delay or prevent optimal cancer treatment. Cardio-oncology programmes aim to prevent such issues by ensuring proper CV management allowing optimal oncology therapy and providing a supportive network throughout the treatment phase.[650] Psychologists, as an integral part of the cardio-oncology team, are essential to help people to cope with the psychological consequences of the disease and treatment. Physiotherapists and dietitians also play vital roles in empowerment and reassurance.

8.5.2. Cancer survivors

After radical anticancer treatment, where a good long-term prognosis is expected, stress may be related to the fear of cancer recurrence,[651] or depression related to the complications of cancer or its treatment.[652] Among childhood cancer survivors, stress/distress was associated with new-onset dysrhythmia (RR 2.87), perceived stress with hypertension (RR 1.42), PTSS and anxiety with dyslipidaemia (RR 1.72 and 1.54, respectively).[653] A significant relationship between severe psychological distress and CVD in cancer survivors was observed (OR 2.95), especially in younger females.[654]

8.5.3. Advanced cancer disease

Awareness of cancer progression can lead to depression, which may be worsened by cancer treatment-related toxicity.[655] Cancer progression, fatigue, and therapy-related toxicity (haematological, endocrinological, neurological and particularly, cardiological) contribute to feelings of discouragement and depression.[656] One in four people with advanced cancer, HF, chronic obstructive pulmonary disease, and/or human immunodeficiency virus/acquired immunodeficiency syndrome may experience mental health issues, including depression, alcohol abuse, PTSD, or anxiety disorders.[657] Such conditions often coexist and may be observed in cardio-oncology.

8.5.4. Cancer therapy-related cardiovascular toxicity

People with pre-existing CVD are more sensitive to cancer therapy-related CV toxicity including CV dysfunction; however, stressors like anxiety can be an additional trigger.[658] People with breast cancer who experienced cancer therapy-related CV dysfunction reported significant declines in physical, social, and psychosocial well-being, including overwhelming fatigue, mental burden of anxiety (fear of death, depression, stress, poor sleep quality), and social challenges (lack of understanding and acceptance).[659] Heart failure in breast cancer survivors is particularly linked to serious mental well-being deficits, especially in the early stages.[660] This underscores the need for multidisciplinary cardio-oncological care models.[659]

8.5.5. Impact of cancer therapy on mental health

People in the cardio-oncology setting may experience neurotoxicity, including chemotherapy-induced cognitive dysfunction ('chemobrain'), particularly with cardiotoxic therapies, which correlates with increased fatigue and psychological distress.[661] Potentially cardiotoxic cancer treatments with possible cognitive impairment include: chemotherapy (doxorubicin, paclitaxel, methotrexate, fluorouracil), hormone therapies (aromatase inhibitors, anti-oestrogen, androgen deprivation therapy), targeted therapies (antiangiogenic therapy), and immunotherapy (anti-CTLA-4, anti-PDL-1).[662]

Androgen deprivation therapy, a primary treatment for prostate cancer, is associated with a higher risk of depression and psychiatric outpatient visits.[663] Endocrine therapy for breast cancer may cause mood disorders,[664] sleep problems,[665] cognitive decline,[666] fear of cancer recurrence,[667] emotional distress, and concern about appearance.[668] Severe fear of cancer recurrence was associated with a higher risk of depression and lower QoL in breast cancer survivors.[669]

Chemotherapy-induced peripheral neuropathy significantly decreases QoL and impacts on mental health. Older (cisplatin and vinca alkaloids) and newer (taxanes, oxaliplatin) anticancer agents can be responsible for these neurological side effects. Oncology expert documents recommend antidepressants (e.g. venlafaxine, duloxetine),[670] but these should be chosen following consideration of CVD risk (e.g. HF or arrhythmias/QTc prolongation). Radiation, while essential in many cancer treatments, can induce CV toxicity[671] and significant mental health issues.[672] The Ontario Cancer Registry showed mental health conditions (anxiety, depression, and low well-being) were associated with higher comorbidity burden during radiation.[673]

8.5.6. Psychological interventions

One of the roles of cardio-oncology is to minimize the barriers to oncological treatment related to a person's CVD. Providing simultaneous cardiology care can improve the psychological well-being of people dealing with both cancer and CVD. Cardio-oncologists should identify

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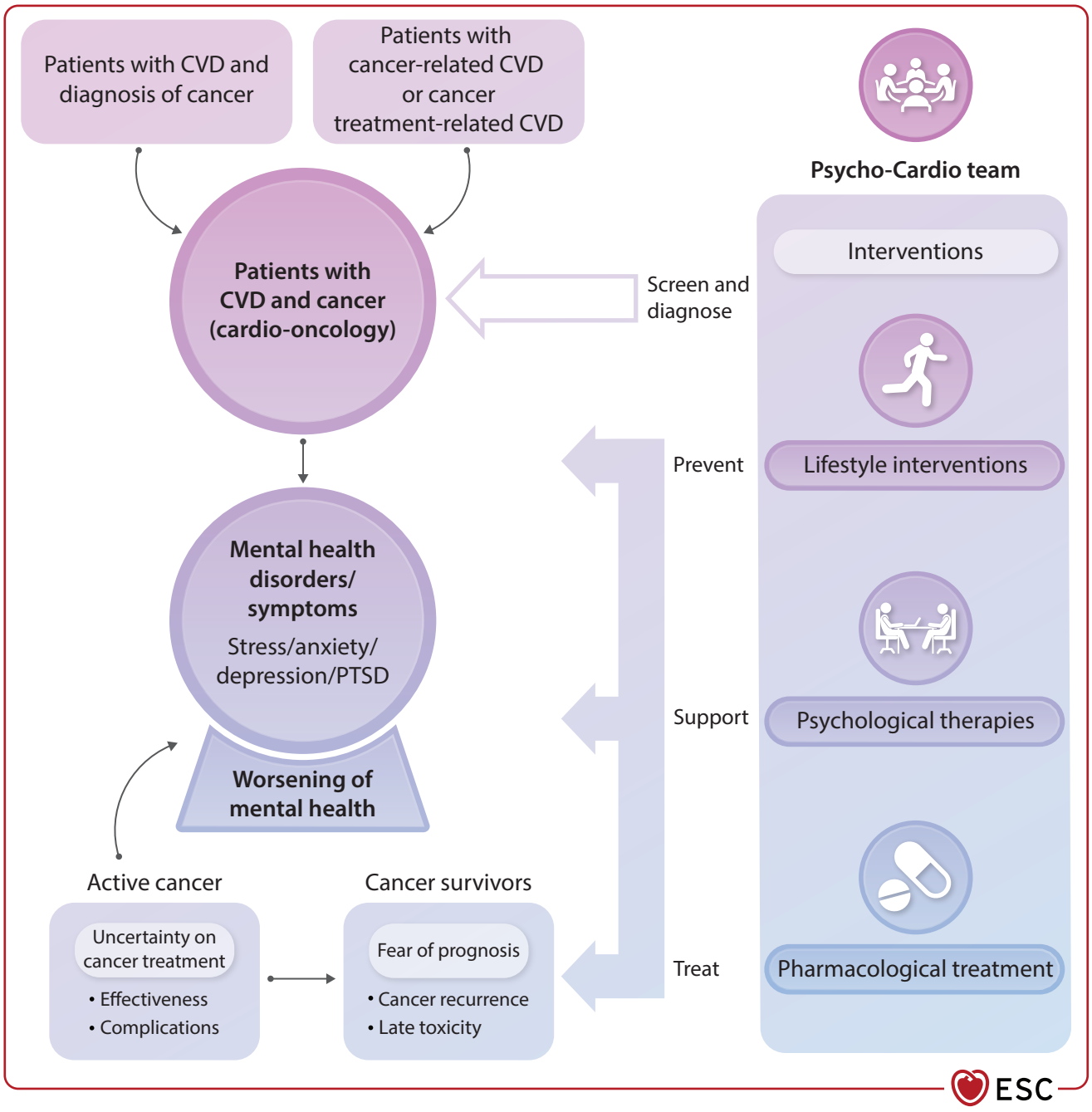

Figure 19 Management of mental health in people with cardiovascular disease and cancer. CVD, cardiovascular disease; PTSD, post-traumatic stress disorder.

psychosocial distress, including depression, anxiety, anger, social isolation, marital/family distress, sexual dysfunction, and substance abuse. People in the cardio-oncology setting may benefit from multidisciplinary team discussions, involving CV specialists, oncologists, and mental health professionals. Alternatively, they should be referred to mental health specialists, who can collaborate with the primary cardio-oncology team to support comprehensive care.[674]

8.5.7. Lifestyle interventions in cardio-oncology

A comprehensive approach is necessary in cardio-oncology, as both CV health and mental health should be monitored during and after cancer therapy. The essence of a cardio-oncology clinic resides in the availability of a doctor to address symptoms related to CV toxicity from oncological treatment or potential cancer relapse/progression, which may coexist.[675] The benefits in cardio-oncology include recommending physical activity:

- Cancer survivors with CVD: an exercise-based programme can improve cardiorespiratory fitness and survival;[676] ECR can improve depression scores in breast cancer survivors.[677]
- In people with advanced or metastatic cancer,[678] exercise interventions can lower mortality, and improve psychosocial function and sleep quality.[679]
- Women with breast cancer receiving potentially cardiotoxic therapies may improve their mental health by a comprehensive CV risk reduction programme.[680]

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8.5.8. Medical interventions (including pharmacological therapies)

There are no specific recommendations or evidence for the efficacy of psychiatric drugs in cardio-oncology. However, data from general cardiology and oncology can be extrapolated and implemented with careful consideration of specific requirements of people with cancer and CVD.

The frequency of ventricular arrhythmias increases in people with advanced cancer,[681] with the risk compounded by coexisting heart disease.[682] Psychiatric drugs (antipsychotics, antidepressants), CV drugs (especially antiarrhythmics), and oncological drugs may interact, leading to QTc prolongation, and increased bleeding risk.[683] Therefore, it is important to avoid significant drug–drug interactions to minimize side effects and prevent reduced effectiveness of cancer treatments due to altered plasma concentrations.[680,683] There are potential positive indirect effects on mental health resulting from CV therapies:

- Treating cancer therapy-related CV dysfunction and cancer-related anaemia may decrease shortness of breath, easing anxiety and distress.[684]
- Treatment of tachycardia/tachyarrhythmia or autonomic dysfunction due to radiotherapy, chemotherapy, or cancer, may improve psychological symptoms.[685–687]

On the other hand, reducing anxiety and stress may lower blood pressure and help control hypertension in people living with cancer. A summary of the major management steps of mental health in cardio-oncology and the main management approaches is shown in *Figure 19*.

8.6. Section summary points and management consensus statements from *Section 8*

SECTION SUMMARY POINTS

(i) Depression, anxiety, and chronic stress show higher prevalence in women compared with men and are associated with increased CVD risk.
(ii) Women with CVD exhibit higher rates of mental health conditions, which are associated with worse outcomes, particularly depression.
(iii) Sex differences in the multidirectional relationship between CV and mental health suggest a role of biological and sociocultural components (gender).
(iv) Evaluation of mental health and frailty in elderly people with CVD is of utmost importance,
(v) Socioeconomically deprived populations show higher rates of CVD and mental disorders and require special attention.
(vi) Cancer, CVD, and mental disorders exhibit significant three-way relationships with shared risk factors.

Continued

MANAGEMENT CONSENSUS STATEMENTS

(i) Psycho-Cardio teams may need to tailor their intervention to the specificities of the target population, with special attention to sex differences, age, frailty, and SES.
(ii) The appropriateness of antidepressants, drug interactions and side effects in the multimorbid, elderly, and frail need careful evaluation by a multidisciplinary team.
(iii) Migrants and refugees may benefit from directed proactive programmes to assess their CV and mental health due to the high prevalence of conditions and their potential difficulties to access the healthcare system.

9. Key messages

(i) The interplay between mental and CV health should be known and acknowledged in order to provide a holistic and integrated care.
(ii) Healthcare professionals should aspire to implement an integrated Psycho-Cardio team approach that is tailored to the local needs.
(iii) The ACTIVE principles (*Acknowledge, Check, Tools, Implement, Venture, Evaluate*) can be used as a practical approach to implement integrated mental healthcare into CV practice.
(iv) Screening for mental health conditions (mainly anxiety, depression, and PTSD) and psychosocial risk factors could help improve CV risk assessment in healthy individuals.
(v) Screening for mental health conditions in people with CVD is important since these are highly prevalent and associated with worse outcomes.
(vi) Initial screening may be performed with a two-item measure, followed by longer validated tools if it raises mental health concerns.
(vii) A stepped care approach for mental health in CVD is advisable: intensity of mental care should be tailored to individual need.
(viii) There is low to moderate certainty evidence that psychological interventions have an effect on depression, anxiety, and QoL in people with CVD. The evidence is weaker or non-existent for a reduction in MACE and mortality.
(ix) Pharmacological treatment with anxiolytics or antidepressants in people with CVD and mental health conditions should be balanced against risks, considering drug–drug interactions and side effects.
(x) Caregivers of people with CVD, who play a key role in well-being and treatment adherence, often face mental health challenges themselves, highlighting the need for strategies to assess and support their mental health.
(xi) People with SMI have a worse CV outcome. Efforts should be made to reduce stigma and provide optimal Guideline-directed CV care, with special attention to treatment adherence and clinically relevant drug–drug interactions.
(xii) Specific characteristics (sex, gender, age, frailty, SES, comorbidities, co-medications) should be carefully assessed as they are modifiers of the interaction between CVD and mental health and may merit individualized approaches.

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10. Gaps in knowledge

There are substantial gaps in the knowledge of the multidirectional relationship between mental health, CV health, and CVD, and its mechanisms. Further, optimal strategies to identify, prevent, and manage mental health conditions in people with CVD are lacking. These gaps not only include finding effective interventions to prevent and manage mental health conditions and ways to implement them, but also ways to change the system to provide integrative healthcare including mental and physical health. A summary of the main gaps across the broad domains covered in this document are outlined below.

10.1. Knowledge gaps in relation to prevention and screening

- There is a lack of evidence-based, cost-effective, and tailored interventions to improve psychosocial factors, mental health conditions, and mental well-being as preventive measures for CVD.
- Determination of optimal screening protocols, including timing, frequency, and methods, for mental health conditions in people with CVD, and how these might vary by condition have not been established.
- Screening-based treatment algorithms are not defined.
- Data on the cost-effectiveness of interventions to identify, prevent, or treat mental health conditions in people with CVD are lacking.

10.2. Knowledge gaps in relation to clinical management

- Feasibility, effectiveness, and sustainability of long-term non-pharmacological interventions, such as physical activity, psychotherapy, and social prescribing need to be established.
- Evaluation of specific psychological interventions and their delivery methods, including digital health solutions, is needed.
- Effective behavioural strategies for achieving behaviour change and improving CV risk profiles among people with mental disorders, including SMI, need to be developed and tested.
- Understanding of the role of trauma-specific prevention or treatments for CVD-related PTSD is lacking.
- Research into the mental health impact of caregiving for people with CVD, prevention of its negative consequences, and integration of interventions into routine CV care is needed.
- Pharmacological research is needed to:
  - Demonstrate the safety and efficacy of antidepressants and antipsychotics in people with HF and their effects on CV clinical outcomes.
  - Explore the role of pharmacogenomics in stratifying treatment to minimize CV adverse effects and enhance psychiatric treatment efficacy.
  - Investigate the efficacy of psychiatric drugs in cardio-oncology.

10.3. Knowledge gaps in relation to special populations

- Cardiovascular risk scores for people with SMI need to be recalibrated.
- Randomized controlled trials of interventions for elderly people with comorbid CVD and mental health conditions are needed.
- The efficacy of multidisciplinary approaches in improving outcomes for people with multimorbidity requires further research.

10.4. Knowledge gaps in relation to healthcare systems and healthcare delivery

- Development and testing of integrated or collaborative care models for people with coexisting CV and mental health conditions is needed.
- Care pathways to streamline the management of people with CVD and mental health conditions need to be developed and evaluated.
- Evaluation of community-level and policy interventions to address socioeconomic disparities impacting CV and mental health is essential.

11. Conclusions

This document provides a comprehensive review of the evidence of the critical interplay between mental and CV health and disease, emphasizing the need to integrate mental health assessment and management into routine CV care. However, the consistency of definitions, mechanisms of interactions, and optimal ways to investigate, prevent, or treat the negative impact of mental health on CVD and vice versa need further research.

Social and clinical efforts are needed to fight the stigma of mental health conditions in the population and in healthcare systems to reduce its impact on CV care. This is particularly urgent for people with SMI, in whom an extra effort is needed to reduce the major gaps in CV prevention, acute and chronic CV care. Awareness campaigns and educational programmes for CV care professionals, people with CVD, their caregivers and decision-makers will be needed.

Integrated CV care models with a holistic view of health need to be co-developed in hospital and outpatient CV care units, integrating and coordinating with mental health professionals, primary care and social care. These should be co-designed together with people with lived experience of CVD and their caregivers, and adapted to the local conditions and availability, individual characteristics and needs. Comprehensive ECR programmes are good examples of care integration. Educational modules and specific training programmes designed by medical and nursing staff and allied health professionals, particularly mental health professionals, are warranted. Reimbursement models for the new models of care need to be addressed and implemented by local authorities.

Future research is needed to increase the knowledge of the multilateral interactions between mental health and CV health and obtain solid evidence for the prevention and management of the negative consequences of these interactions. This should include prospective longitudinal studies in the population, in people with different CVDs, and in people with mental health conditions, including those with SMI. There is an urgent need for RCTs, with larger and more diverse samples of individuals and types of CVD that test the effectiveness and safety of medical and non-medical interventions. These trials should include psychological, pharmacological, social, and other types of interventions to prevent or reduce negative mental and CV outcomes.

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12. Summary of mental health aspects in specific cardiovascular diseases

Summary information for the CVDs discussed in this consensus statement is provided in Supplementary data online, *Tables S12–S17*.

13. Clinical cases and patient perspectives

Clinical cases and patient perspectives are available at *European Heart Journal* online.

14. Evidence tables

Evidence tables are available at *European Heart Journal* online.

15. Data availability statement

Supplementary data are available at *European Heart Journal* online.

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17. Appendix

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